

Exhibit 1

IN THE UNITED STATES DISTRICT COURT
IN AND FOR THE DISTRICT OF DELAWARE

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INTEGRA LIFESCIENCES CORP., : CIVIL ACTION
INTEGRA LIFESCIENCES SALES :
LLC, CONFLUENT SURGICAL, :
INC., and INCEPT LLC, :

Plaintiffs, :

vs. :

HYPERBRANCH MEDICAL :
TECHNOLOGY, INC., :

Defendant. : NO. 15-819 (LPS) (CJB)

- - -

Wilmington, Delaware
Thursday, December 1, 2016
2:03 o'clock, p.m.
***Telephone conference

- - -

BEFORE: HONORABLE CHRISTOPHER J. BURKE, U.S. MAGISTRATE
JUDGE

- - -

APPEARANCES:

YOUNG, CONAWAY, STARGATT & TAYLOR LLP
BY: KAREN L. PASCALE, ESQ.

-and-

Valerie J. Gunning
Official Court Reporter

1 **APPEARANCES (Continued):**

2 **BANNER & WITCOFF, LTD.**

3 **BY: ROBERT F. ALTHERR, ESQ. and**
4 **CHRISTOPHER B. ROTH, ESQ.**
 (Washington, DC)

5 **Counsel for Plaintiffs**

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7 **MORRIS, NICHOLS, ARSHT & TUNNELL LLP**

8 **BY: THOMAS C. GRIMM, ESQ.**

9 **-and-**

10
11 **COOLEY LLP**

12 **BY: ADAM M. PIVOVAR, ESQ.**
 (Washington, DC)

13 **Counsel for Defendants**

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15 **- - -**

P R O C E E D I N G S

(REPORTER'S NOTE: The following telephone conference was held in chambers, beginning at 2:03 p.m.)

THE COURT: Good afternoon, counsel. It's Judge Burke here.

Before we get started, let me just say a few things for the record with everyone on the line. The first is that we're here today for a discovery dispute teleconference in the matter of Integra Life Sciences Corporation, et al versus HyperBranch Medical Technology, Incorporated. This is Civil Action No. 15-819-LPS-CJB here in our court.

And because we're here today on the record for our call, I have with me a court reporter from the court who will be taking down our call today. And so I'd ask counsel if they would identify themselves before they speak. It will help us make sure we get a good and accurate record of our all this afternoon.

With all that said, let me ask counsel to identify themselves for the record before we go further. Let's begin with counsel for the plaintiff and there, let's begin with Delaware counsel.

MS. PASCALE: Good afternoon, your Honor. It's

1 Karen Pascale from Young Conaway for the plaintiffs, and
2 with me on the line from the Banner & Witcoff firm are
3 Robert Altherr and Christopher Roth, and Mr. Altherr will be
4 presenting argument today.

5 THE COURT: Okay. Thank you. And good
6 afternoon.

7 And who is on the line for defendants' side?
8 Again, let's begin with Delaware counsel.

9 MR. GRIMM: Good afternoon, your Honor. It's
10 Tom Grimm at Morris Nichols here in Wilmington, and on the
11 line with me is my co-counsel, Adam Pivovar, of the Cooley
12 firm.

13 THE COURT: Okay. And to you all, good
14 afternoon as well.

15 Counsel, we have two sets of discovery disputes.
16 We have disputes raised by the plaintiff, and there are a
17 number, and then we have a dispute raised by the defendant,
18 of which there is really one. And partly because there's
19 just one and it's a little more discrete, I think I will
20 start with the defendants' dispute first and then we'll move
21 over to the plaintiffs' side.

22 I'm going to assume, by the way, that none of
23 these disputes have been resolved since they've been raised
24 with me, but as we start talking about them, if the parties
25 know they've been talking about the disputes and they have

1 resolved some of them or they know they can easily be
2 resolved, please jump in and let me know.

3 All right. With regard to the defendants'
4 dispute, there, the initial letter was set out in DI 204,
5 that dispute, I'm sorry. Not DI 204. I apologize. DI 199
6 is the document that includes the defendants' discovery
7 dispute.

8 There, defendants are faulting plaintiff with
9 regard to plaintiffs' response to defendants'
10 Interrogatories Number 1 and 2 for failing to identify the
11 individuals who contributed to the conception of the
12 inventions described in the patents-in-suit and for failing
13 to address in their responses in a certain priority date for
14 the claims on a claim-by-claim basis.

15 On that front, let me actually turn to plaintiff
16 first, because I think the gist of plaintiffs' response as
17 to why they are not required to do more than what they've
18 done in their responses is found on page 2 of plaintiffs'
19 letter in the second full paragraph where they say, if
20 there's no specific reference that a patentee is trying to
21 antedate, then the information sought by defendants'
22 interrogatories is not even relevant.

23 What I take that to mean is that the plaintiffs'
24 position is unless the defendants have actually pointed to a
25 reference that predates the presumptive priority date of the

1 patents, we don't have to answer more specific questions
2 about exactly what that priority date is, or whether or not
3 on a claim-by-claim basis it's anything different from the
4 presumptive priority date.

5 I guess, Mr. Altherr, I will turn to you and
6 explain first, have I accurately stated your position? And
7 if I have, can you tell me what authority you have to
8 support the position that you're taking there?

9 MR. ALTHERR: The patent is presumptively valid,
10 your Honor, and the presumed date of invention is the filing
11 date. All right. And until they have done something to
12 come in to put in issue the validity of the patent, raising
13 it prior to that filing date, there's a conception, the
14 conception is not relevant and the earlier priority dates
15 are not relevant.

16 We can rely upon our date of resumption. Now,
17 we did indicate there, too, your Honor, we did give them who
18 were the inventors that contributed to the claim and
19 indicated that we were going to be relying, at least
20 currently, on our filing date. If they put in issue to
21 raise it to an earlier one, then we would go ahead with
22 those claims where it was raised and we could go in and
23 answer the specific questions.

24 THE COURT: And I understand that at least at
25 the present time, I think your position is going to be

1 that the presumptive priority dates, say the filing dates
2 with regard to the patents are the priority dates, but just
3 on the question of relevance, you know, because what
4 defendant wants to know is, they want to nail you down in
5 terms of your position right now, and what they are saying
6 is, look. If we've alleged that the claims are invalid,
7 then that necessarily makes relevant, i.e., puts at issue,
8 you know, what is the actual priority date for each of these
9 patents?

10 And even if we have not yet cited to a prior art
11 reference that predates those presumptive dates, it's
12 relevant to know exactly what the plaintiff thinks those
13 dates are and to get an answer from them because it's always
14 relevant to know exactly what the priority date is said to
15 be because it always relates to what prior art can be
16 asserted. They've cited to the McKesson case for that
17 proposition and there are other cases that cite to McKesson
18 for a similar one.

19 I guess what I'm asking you is: What case
20 support or other support do you have for the proposition
21 that questions about the priority date or the conception of
22 the invention aren't relevant until the defendant points to
23 a piece of prior art that predates that presumptive priority
24 date?

25 MR. ALTHERR: As far as the -- it's very

1 well-known, your Honor, that they have the burden of proof
2 on the issue of invalidity, and until they have put it at
3 issue, all right, we can rely upon the presumptive date,
4 and they have not put it in issue.

5 THE COURT: Well, they've certainly put
6 invalidity at issue in the case. They have raised the
7 defense of invalidity, haven't they?

8 MR. ALTHERR: Could I let my co-counsel,
9 Mr. Roth, address this one point for your Honor?

10 THE COURT: Sure. Absolutely. Mr. Roth?

11 MR. ROTH: Thank you, your Honor.

12 One example where they may even put at issue
13 invalidity, but still priority dates are immaterial, are,
14 for example, if they are basing invalidity on materials that
15 are more than even a year prior on any possible priority
16 documents.

17 If they are relying on prior art references from
18 the seventies or the sixties or the fifties or however far
19 back in time you want to go, what the actual date of
20 conception and entitlement to priority is immaterial because
21 there's no documents in the chain, the patents-in-suit, that
22 goes back before the eighties, or the seventies, or the
23 sixties.

24 THE COURT: Right. But I guess my question is:
25 Isn't it always, as long as invalidity is in the case, isn't

1 it always, quote unquote, "relevant" as to what the
2 patentee's position is as to what the effective priority
3 date is in a case, because you are always, as the defendant,
4 are going to need to know what is the lay of the land here
5 with respect to prior art and questions of invalidity.
6 So you're always going to want to know, and you're always
7 going to assert it's relevant to the defenses to know
8 exactly what the position is as to, you know, what's the
9 first date from which we have to look earlier for relevant
10 prior art.

11 MR. ROTH: Well, no, your Honor. In that, we
12 don't -- the burden on us is we can presume the patent's
13 filing date is the date of invention, and until they beat
14 that, the rest, everything else is not at issue in the
15 case. They have to come up with something earlier than
16 the filing date or they have not even put invalidity at
17 issue.

18 THE COURT: I'm not sure I understand what you
19 mean by that last statement, they have to come up with
20 something earlier than the filing date or they have not put
21 invalidity at issue?

22 MR. ROTH: Yes. If they have not -- if they
23 can't come up with a reference that beats the presumptive
24 invention date, which is the filing date, they have not put
25 invalidity at issue. All right?

1 And, now, if they came up with a reference, all
2 right, which was a reference which would allow -- how shall
3 I say it, a reference that would be, say, intervening in
4 between the earliest priority claimed on the face of the
5 patent and the actual filing date, then obviously they have
6 put into issue, all right, what is the earliest filing date.
7 But they have not identified anything like that.

8 THE COURT: Okay. Let me just turn to the other
9 side. Go ahead.

10 MR. ROTH: Another thing, your Honor.

11 THE COURT: Sure, Mr. Roth.

12 MR. ROTH: Once we know what they are asserting
13 for invalidity, we've already said, and we said it, we will
14 within five days of getting proper claim construction
15 charts, we'll supplement and provide them all of that
16 information.

17 THE COURT: Right. Okay. And, again, my
18 question is: Why haven't they already made the request
19 relevant by nature of simply alleging that the claims are
20 invalid? And I think I understand your position. Let me
21 just turn to Mr. Pivovar.

22 Mr. Pivovar, I think I am making your argument
23 in your papers, but is there anything I've said so far that
24 is not the argument you're making?

25 MR. PIVOVAR: Your Honor, I believe that the

1 gist of it is effectively correct. One of the issues is
2 your invalidity at least under 102 and 103 for anticipation
3 and obviousness based on prior art.

4 And to determine whether art is prior, we need
5 to determine what the priority date is they are asserting on
6 a claim-by-claim basis, and I think that's obviously
7 something you understand and you are asking plaintiffs
8 about.

9 The only second part about that I would really
10 take a little bit of issue with is their characterization of
11 us not having put these intervening dates and what their
12 actual dates of invention and priority are at issue. We've
13 identified to them numerous references that fall in these
14 intervening claim periods that if they are going to try to
15 antedate, they should do that now, and their allegations
16 that we have not put that at issue just simply aren't true,
17 your Honor.

18 And I would also point out that during the
19 preliminary injunction phase, this issue came up as well,
20 and it wasn't until they finally had their expert reports in
21 that they gave us what their priority assertions were, and
22 we don't want to necessarily be in that position again where
23 they're filibustering us a little bit on discovery and what
24 our priority is and then we get it all then.

25 So really, as your Honor recognizes, it is

1 just a matter of let's get it out front, let's see what
2 your positions are. Let us know what your dates are so
3 we can evaluate what the prior art actually is with respect
4 to those dates. And, finally, we did put that all into
5 issue with the art that we've cited in our invalidity
6 contentions.

7 THE COURT: And just to kind of give us an
8 example so we can just talk about this in in a practical
9 sense before we finish up, can you give me just roughly --
10 I'm not looking for the exact date, but as to a particular
11 patent-in-suit, you know, can you just give me an example,
12 like, Judge, for example, with respect to the X patent, the
13 presumptive filing date, i.e., the date of the filing of the
14 application at issue would be X. And so we've cited prior
15 art that predates that date, you know, for example, we've
16 cited, blah, blah, blah.

17 Now, we need to know, though, if the plaintiff
18 is going to assert that the invention was conceived earlier,
19 because if they're going to try to move that priority date
20 back and X out some of the art we've cited, we need to know
21 that.

22 Is that the gist? And can you just give me an
23 example of how this might play out in real life here?

24 MR. PIVOVAR: Your Honor, that is exactly the
25 gist. I will give you one example and that is the '034

1 patent has a filing date of November 9th, 2001. The '034
2 patent is a continuation in part of two different patent
3 chains.

4 So those are priority documents that predate
5 those that go back to 1998, and in the chain there's
6 actually some that go all the way back to 1997, and maybe
7 even as early as '96.

8 Now, it's our position and always has been, and
9 this is something we argued during the preliminary
10 injunction phase, that the plaintiffs cannot get an earlier
11 priority date than the November of 2001 filing date for the
12 '034 patent, but what they did is they argued in the
13 preliminary injunction phase after we put in art that was
14 intervening, that they could actually try and square behind
15 and get an earlier date.

16 Now, that same piece of prior art we put into
17 our invalidity contentions along with a slew of other art
18 that falls within this 1996 to 2001 time frame to force them
19 to tell us, hey, what is your priority date? Can we rely on
20 these as a matter of substance or are we going to have a
21 fight as to whether or not this is going to be prior art?
22 So that's one specific example, your Honor.

23 THE COURT: Okay. And I'm sorry. In the
24 example you raised, the 1998 or 1997 dates, what were those
25 dates corresponding to?

1 MR. PIVOVAR: It would be helpful I think in a
2 way if we still had the slides from the preliminary
3 injunction case, but the relationship of all of the patents
4 in this family are somewhat complex and there have been a
5 lot of applications that have been combined together.

6 In essence, the '034 patent is a continuation
7 from two different patent applications, which themselves are
8 combinations of either an individual, in the one instance,
9 individual provisional application or a combination of three
10 or four different prior applications.

11 So it gets a little complex in terms of which
12 one they are actually pointing to, which actual provisional
13 application they're trying to rely on to support their
14 priority date. And in a sense, your Honor, this is really
15 why we need to have these interrogatory answers, so that we
16 can understand within this complex milieu of all of these
17 different provisional applications what is it they're
18 actually saying supports the earliest date of their claims.

19 THE COURT: And the November 9th, 2001 date,
20 that is the date of the application that you believe is the
21 correct one to look to for the filing date at issue?

22 MR. PIVOVAR: Yes. So in our view, that -- so
23 that's the filing date of this specific application.

24 THE COURT: Okay.

25 MR. PIVOVAR: That's the presumptive date of

1 priority, and then we believe that they are unable to get
2 anything earlier than that, but if they're going to try, we
3 would like to know exactly what is the basis for them to do
4 so and what is the priority information they are going to
5 rely on.

6 THE COURT: Okay.

7 MR. PIVOVAR: That's right.

8 THE COURT: All right. Mr. Altherr, anything
9 else on your end before we finish this issue?

10 MR. ALTHERR: Okay. With respect to the
11 specific example he talked about, your Honor, that came up
12 during the preliminary injunction phase, and we did, in
13 fact, supplement our interrogatory to provide the
14 information on that issue, and additionally, it was provided
15 in Dr. Mason's rebuttal report on that particular patent.
16 They had that already.

17 THE COURT: What about Mr. Pivovar's contention
18 that with regard to the need to cite prior art that has a
19 date that makes relevant the question of what, in fact, is
20 the priority date at issue here? You know, he says, you
21 know, they are taking the position that as to the '034, it's
22 a November 2001 date. They've cited art that predates that,
23 but that may be arguably might fall after a date of some
24 other related application that they are worried the
25 plaintiff might point to as the date that matters.

1 Why haven't what they've done already, for
2 example, as to that patent been enough to put at issue and
3 make relevant the issue even under your explanation of what
4 relevancy means?

5 MR. ALTHERR: All right. First of all, your
6 Honor, as he indicated, you have to take each claim to
7 determine its date of invention. The art that they have
8 cited in that, they have not applied to any claims. All
9 they've done is throw together a big bucket of references
10 and said, some are anticipated, but they have not identified
11 one that anticipates any of the claims. They said some are
12 obvious in that, but they have not identified them as to any
13 specific claim in that.

14 So we don't know what prior art they're
15 asserting against what particular claims and what type of
16 combination to really put that in issue.

17 THE COURT: Okay. So your response in part is,
18 we think for various reasons their invalidity contentions
19 are deficient, so we think they have not asserted an
20 invalidity position on a claim-by-claim basis, i.e., citing
21 references as prior art on a claim-by-claim basis, and so
22 therefore we don't think they've done enough to, quote, "put
23 at issue?"

24 MR. ALTHERR: Absolutely, your Honor.

25 THE COURT: All right. I think I have a handle

1 on that. Let me give you my decision on this issue because
2 it's one I can decide now and it is discrete enough, and
3 that is that I'm going to grant the defendants' motion for
4 relief and require the plaintiffs to provide the
5 supplemental responses that HyperBranch has requested. That
6 is, I'm going to require that the plaintiff provide
7 supplemental responses to HyperBranch's interrogatories
8 Number 1 and 2, and in doing so, to specify in those
9 responses the individuals who contributed to the conception
10 and the asserted priority date for the claims on a
11 claim-by-claim basis.

12 I disagree with plaintiffs' position that those
13 responses aren't relevant until the defendant has, quote,
14 "put at issue a relevant piece of prior art by citing to
15 some reference that is alleged to," quote, "put the
16 reference at issue."

17 I think based on the authority that the
18 defendant has cited, when the defendant asserts a defense of
19 invalidity, and here in particular we're talking about a,
20 for example, a defense under 102 and 103, that that
21 necessarily makes relevant the priority dates for each of
22 the claims of each of the patents at issue. It's an
23 important issue in the case at that point when the priority
24 date is for those claims, so that the accused infringer can
25 know as to what date it must use as its target to find prior

1 art that precedes that date that might be potentially
2 invalidating.

3 I think that basic position is set out in the
4 McKesson case that's cited in the defendants' letter and
5 also in other cases, for example, that cite McKesson,
6 including Blast Motion, Incorporated, versus Zepp Labs
7 Incorporated, which is found at 2016 Westlaw, 510, 7677, a
8 case out of the Southern District of California.

9 And so I think that the information that the
10 defendants are seeking as to asserted priority dates on a
11 claim-by-claim basis and individuals who contributed to the
12 conception of the claims is relevant to a defense in the
13 case, and the plaintiffs have not sufficiently responded to
14 the gist of the interrogatory and they should be required to
15 do so. So I will require that they be ordered to supplement
16 the responses by the requested date that's on or before
17 December 9th of 2016.

18 All right. Let me turn now to the plaintiffs'
19 disputes, and there are a number. And let me try to
20 summarize what I understand to be those disputes, and
21 then let me then ask the parties for their positions on
22 them.

23 And so, first, the plaintiff is asserting that
24 the defendants' invalidity contentions under Sections 102
25 and 103 and invalidity contentions under Section 112 are

1 deficient.

2 Next, the plaintiff is asserting that responses
3 to certain interrogatories by the defendants are deficient.
4 There, I understand particularly the responses to
5 Interrogatory Number 1, which is seeking noninfringement
6 contentions, as well as Interrogatory Number 3, which is
7 seeking information about contributory infringement, and
8 Interrogatory Number 8, which is seeking information
9 relevant to whether certain instructions as to how to use
10 the products at issue were followed, which in turn relates
11 to allegations of indirect infringement.

12 So a couple different buckets of disputes here.
13 Let's start with the dispute over the sufficiency of the
14 defendants' invalidity contentions.

15 Mr. Altherr, let me turn to you first and let me
16 ask a question or two, and then I will make sure you add
17 anything you want to add as to your position here.

18 On this front, and I guess I'm focusing at least
19 at first on the 102 and 103 issues, and I understand, I
20 think, what your complaint is there. It is that although
21 the response is a lengthy one in terms of pages and includes
22 as to claim terms and claim elements citation to a number of
23 pieces of prior art, you would think that the defendant
24 hasn't specifically articulated how under either 102 or
25 103, particular certain pieces of prior art are being

1 utilized to assert that a particular claim is invalid and
2 that they have to do a more specific articulation in that
3 regard.

4 Am I right, and is there anything more that you
5 want to add to your position?

6 MR. ALTHERR: Yes, your Honor, you're correct.
7 Basically, we see there are four issues that they say that
8 the claims are anticipated, but they don't identify what
9 particular claims are anticipated or what particular
10 reference is the anticipatory reference.

11 The second one is that they assert that certain
12 claims are obvious, but they don't say which claims are
13 obvious, and they don't identify any particular references
14 or particular combinations of references that invalidate any
15 particular claim. They don't show -- you have to do
16 obviousness of the claim as a whole. So even their chart
17 where they combine, they show certain combinations -- not
18 combinations, where certain things are found in the prior
19 art doesn't show any invalidity of a claim, of any claim as
20 a whole.

21 And the other thing is that they've got
22 information in there that they call state of the art, but
23 they have not distinguished between prior art they're
24 relying on for invalidity and what they are saying is the
25 state of the art.

1 THE COURT: And you also assert as to 103, they
2 have not articulated what is the motion to combine any two
3 or more references that are asserted to give rise to an
4 obviousness challenge. Am I right?

5 MR. ALTHERR: Yes, your Honor, that is correct.

6 THE COURT: All right.

7 MR. ALTHERR: Do you want to take each one of
8 these as we go or do you want to go into the 112?

9 THE COURT: Well, just on these issues as to 102
10 or 103, you know, a part of the defendants' response could
11 be, and I think it could be, look, the plaintiff, you know,
12 provided its infringement contentions, and I know you've
13 cited to those in the level of detail provided there, and I
14 think in particular you cited to the infringement
15 contentions that are found at DI 10 on the docket, which
16 kind of accompanied your initial complaint and preliminary
17 injunction motion, and those are lengthy and detailed.
18 But didn't those two leave something to the imagination?
19 In other words, you know, isn't, in essence, what you did
20 there was to identify a particular claim elements, and then
21 to kind of like put in the box lots of particular quotes
22 either from literature of the defendants or from your
23 expert reports and kind of leave the defendant a little
24 bit to figure out exactly, well, how is each one of these
25 things asserted to relate to the particular words of the

1 claim?

2 And so why isn't the nature of the defendants',
3 you know, admittedly voluminous response here in their
4 Exhibit A, why isn't that the counterpoint in terms of what
5 you've done in terms of your initial infringement
6 contentions, leaving a little to the imagination but
7 providing a lot of detail.

8 MR. ALTHERR: First, we've got different
9 statutory bases. The first one is 102, anticipation.
10 There's nothing in there that they've provided to leave to
11 the imagination to identify which reference it is they say
12 is an anticipatory reference. There's nothing in there we
13 can find that says which of the asserted claims is asserted
14 to be anticipated. All right?

15 So if they have -- they are playing games. If
16 they have an anticipatory reference, why don't they identify
17 it as an anticipatory reference and tell what claims it
18 anticipates?

19 The same thing with regard to obviousness. If
20 they have a single reference that renders it obvious in
21 that, tell us you've got a single reference. That's all
22 that you need. Show us that reference to that. Show us
23 where it is and identify what claims that it renders
24 obvious.

25 If they're relying upon a combination, tell us

1 what the combination is. Don't play games and tell us, you
2 know, you've got up to a million combinations here and that
3 you figure out what we're trying to say.

4 They pled that these were invalid and said that
5 they are invalid for anticipation and for obviousness, but
6 they won't tell us which claims are invalid for
7 anticipation, which ones are invalid for obviousness and
8 why.

9 THE COURT: Okay. And I guess if they say, you
10 know, look, of course, there could always be more
11 specificity, but, Judge, if you want to understand a little
12 bit of the why here, we're talking about 105 claims.

13 Now, look, plaintiff had a choice. They could
14 go forward on 105 claims at this stage. They're not
15 required to cut it down until later, but, come on. If you
16 want to go forward on 105 claims at this stage, you have to
17 expect -- A, you have to expect us, defendants, to put forth
18 real effort here, to make a solid effort to respond.

19 But 105 claims? You know, I mean, that's what
20 we're hearing from the defendants, and couldn't you have
21 made your case here a little bit easier if you had done
22 something to narrow this field? Wouldn't you acknowledge
23 105 is a lot of claims at this stage to be required to
24 respond to?

25 MR. ALTHERR: We provided -- they should respond

1 in the same level of detail that we provided. We identified
2 at least all of the claims that were infringed. We want to
3 get rid of those claims, and the way we can do it is that if
4 they can identify where it's arguable or where it's
5 questionable on issues on validity. Of course, we're going
6 to drop those claims. All right?

7 And so but they do need to answer those. And
8 they don't have 400 anticipatory references. And it's
9 ludicrous to suggest that they would.

10 THE COURT: Right.

11 MR. ALTHERR: They can identify what's an
12 anticipatory reference. They have some idea having gone
13 through this that they have an idea of what their defenses
14 are, and what it appears they've done is taken every
15 reference that's listed on the face of all of the patents
16 and any references that they got in a search and just
17 through them down and listed them.

18 THE COURT: Well, in fairness, they've done more
19 than that. Right? They have as to each -- well, as to each
20 claim term, because they didn't do it because of asserted
21 redundancies in the claims, they didn't do it as to one
22 claim and then the next and then the next. But they have
23 not only pointed out particular references, but they have
24 pointed out particular language from each reference that I
25 understand is meant to in some way correspond to the

1 language at issue from the claims. Isn't it fair that
2 they've done at least that?

3 MR. ALTHERR: They have taken certain
4 references, a limited number as an example, and said that
5 with respect to those, you can find certain elements of the
6 claims in those examples.

7 As your Honor knows, most inventions are all a
8 combination of known elements, so you're going to be able to
9 take any invention in that and you get enough references out
10 there, you can pull them all together and say, I find this
11 one here, this one here and this one there. That doesn't
12 make the case of obviousness or anticipation.

13 That's what they have alleged. They should be
14 able to at least put aside, what is their anticipation
15 argument? What is their anticipation defense? What is
16 their obviousness defense?

17 THE COURT: Okay. Fair enough.

18 And we'll kind of go -- we'll take first this
19 issue of the alleged deficiencies in the invalidity
20 contentions. Is there anything you want to say about your
21 allegations as to why the contentions as to Section 112 are
22 deficient?

23 MR. ALTHERR: Yes, your Honor. All right.

24 On 112, what they asserted was, they listed I
25 think 138 different claim terms and limitations and said

1 that the terms rendered the claims invalid as to either
2 indefinite or lack of written description or enablement or
3 some -- its and/or, or some combination. Well, we don't
4 know which one applies to which of these. All right?

5 If they're going to assert an indefiniteness
6 defense, they should identify the claim that's indefinite
7 and the term that renders it indefinite, and if it's the
8 written description, they should identify that, if the
9 written description renders the particular claim -- I'm
10 sorry, lack of written description renders a particular
11 claim invalid. They didn't do that. We have no way of
12 knowing or guessing what particular defense they're
13 asserting to any of these claims under 112.

14 THE COURT: And I gather part of your argument
15 is, really, 138-plus limitations are indefinite? That can't
16 possibly be the position. I mean, is that some part of the
17 reason why you listed that number?

18 MR. ALTHERR: Well, your Honor, as far as we're
19 concerned, we're certainly not going to try to present this
20 at trial.

21 THE COURT: Right.

22 MR. ALTHERR: I mean, we'd be laughed out of
23 court. I think, once again, it's just showing they want to
24 play games, are trying to hide the ball. They are not
25 making an honest effort to present, these are what our

1 invalidity contentions are. If they would do that, we could
2 narrow these issues that they have to go forward.

3 THE COURT: All right. Mr. Pivovar, let me let
4 you respond on the allegedly deficient invalidity
5 contentions issue and then I will follow up with a couple
6 questions.

7 MR. PIVOVAR: All right. Thank you, your
8 Honor.

9 I mean, one of the issues we have, and I think
10 you've highlighted this, these are initial. They're
11 preliminary contentions and they're in response to 105
12 different claims.

13 We know that the case is going to be narrowed
14 and further refinement of the parties' positions is going to
15 happen as we move forward, and, in fact, it already has at
16 some level.

17 Considering the plaintiff has selected their 36
18 claims for assertion, at this time were going to be provided
19 you, or at least each other with the claim terms, and we're
20 going to start to narrow the case down.

21 What we tried to do is give them sufficient
22 notice to accomplish what they've said they needed to
23 accomplish from the contentions that we provided. What they
24 said was, we need to know what the prior art said so that we
25 could have some idea of how we can narrow this down to 36

1 claims, and we've tried to do that. We've tried to do that
2 both with respect to the art we've cited, the charts, and
3 where you can find the claim elements in the charts.

4 And I think that our charts have given them a
5 very detailed explanation of where the art discloses each of
6 these elements and how they can evaluate that to get to the
7 36 claims that they've obviously already selected.

8 On that side of it -- I'm sorry, your Honor. Go
9 ahead.

10 THE COURT: I was going to say, why would it not
11 have been necessary though for you at a minimum, albeit, I
12 mean, the 105 claim argument, I understand it, and certainly
13 at some level it has to be a basis for you to be able to say
14 enough is enough. But at a minimum, in terms of
15 Mr. Altherr's request that, for example, as to the Section
16 102 or 103 issues, and at a minimum, we think we're entitled
17 to some assertion that, look, as to this claim, we are
18 asserting that there's an anticipation argument here as to
19 this reference, or an obviousness argument as to these. Why
20 not at least be required to do that?

21 MR. PIVOVAR: Well, your Honor, I think that
22 that is obviously going to happen. It's just a matter of at
23 what point in time does it happen, and then do we have to go
24 back and do that for all 105 claims at this point in time
25 considering we've already gotten plaintiffs' selection of

1 36, or do we move forward from where we are?

2 They've seen all the art. They know what it is
3 all is. And then when we get to 36, and then as time goes
4 by, that's going to narrow down, then we're going to sharpen
5 up our case. We're going to have to be narrowing the number
6 of pieces of art that we can rely on in about
7 three-and-a-half, four weeks, three weeks or so.

8 So I mean that's only going to come into focus,
9 part of the schedule, I think, from this initial 105 claims
10 to our view is, we need to tell them what all of our art is,
11 what all of our potential arguments are, so that we look at
12 it and narrow down so we're not left in a Catch 22 where
13 they are going to come back later and say, oh, you didn't
14 disclose enough. You didn't tell me specifically you were
15 going to apply this in a certain way, and now we're left on
16 the other side of that where they're going to say, well, we
17 didn't adequately disclose it earlier and now we're changing
18 positions.

19 So from our perspective we are trying to be more
20 all-inclusive when, frankly, you know, the case was
21 completely open, and as it whittled down over time, those
22 steps and those refinements are built into the schedule to
23 happen.

24 THE COURT: Right. But obviously from the
25 perspective that you know that I was requiring that there

1 be, you know, sufficiently complete initial invalidity
2 contentions, you know, whatever that looks like, but before
3 the plaintiff makes their cut-down and even currently, the
4 status quo, although they've cut it down to 36, I've allowed
5 that if I find the contentions that you provided deficient,
6 that they'll have the ability to revise that.

7 So the answer can't just be, well, look, we're
8 down to 36, so we can do better now. It has got to be what
9 we did as to the 105 is enough. And both with regard to the
10 102 and 103 issues and the 112 issue, you know, what the
11 plaintiff is saying is, look, at a minimum, we can expect
12 even with a lot of claims, we can expect not just a listing
13 of art or a listing of terms that are asserted to be
14 indefinite, but some nod towards the particular statutes at
15 issue. With 102 and 103, it would be a nod towards are we
16 talking about anticipation or obviousness, and as to what
17 references? As to 112, it would be what part of 112 are we
18 talking about?

19 Why would it have been unduly prejudicial to do
20 that at the stage where you were at 105 claims?

21 MR. PIVOVAR: Just to dial it back to the 102,
22 103 issues, you know, we gave them charts. We gave them on
23 an element-by-element basis. If there are any references
24 that meet all the elements of the claims in our charts, that
25 would be anticipatory. The ones that don't, it would be

1 obviousness. That information is there and can be gleaned
2 with from what we have, and that's why we did it that way.

3 On the 112 front, the issues really are a little
4 bit premature. This is another one of those Catch 22. We
5 just gave them what we could see potentially being all of
6 the issues that could come about based on what we know from
7 the experience with the preliminary injunction phase.

8 As your Honor may recall, one of the big issues
9 we had throughout that phase was they are applying their
10 claims in a way that would render them indefinite if the
11 claims are construed that way. And there are a lot of
12 redundancies across all of the claim terms, so when we
13 identify, like, all of the different language that we say
14 potentially could be indefinite, that number is going to go
15 up, not because the issue is a large number of issues, it's
16 a single issue, but it applies across a large number of
17 different claim elements.

18 Now, also as part of the preliminary injunction
19 phase, we did say how they are applying the claim terms
20 causes them to lack written description and enablement
21 because the bounds of the claims can't really be discerned.
22 So that's how that comes into play.

23 But my point with both of those, your Honor, is
24 that those are issues that are going to be fundamentally
25 claim construction-based issues, that if your Honor resolved

1 the claim construction disputes that we're going to have as,
2 you know, in favor of our position, then those issues may
3 all be resolved, and if you don't, then we'll have to see
4 what the claim construction is and then go from there on how
5 we push our indefiniteness or lack of written description or
6 lack of enablement.

7 So what our goal is on the 112 front is, they
8 know what a lot of our arguments are from the preliminary
9 injunction phase. They know how we've been pushing the
10 argument that they're asserting their claims in ways that
11 cause problems, and because of that, you run into these
12 112 issues and we listed them out.

13 It's our view that we gave them notice, here's
14 all the ones we think could be there, and once we get into
15 claim construction and those issues get resolved, we'll be
16 able to go from there and really kind of narrow down the
17 issues and get to where we are. But it's premature before
18 we get the claim construction decision.

19 THE COURT: It sounds like what you are saying
20 is you really can't have contention interrogatory discovery
21 on Section 112 until you get a claim construction order in
22 any case. Is that your position?

23 MR. PIVOVAR: No, your Honor, that's not my
24 position. I mean, the problem we have is that we have so
25 many claim terms, so many issues and so many disputes, to do

1 it for all 105 claims, once we're like, here's the notice,
2 here's the terms we believe you have problems with. But to
3 go in and actually do that for all of those when we have at
4 the doorstep a couple of narrowing things for 36 claims and
5 then the claim construction that we're going to be doing is
6 going to substantially narrow that and resolve a lot of the
7 issues that we have.

8 THE COURT: Okay.

9 MR. PIVOVAR: Again, these are just initial
10 contentions, your Honor. 112 issues are issues that
11 typically, like, initially don't get the same kind of
12 fulsome disclosure that you get from the prior art. They
13 tend to be ones that come later in discovery because you do
14 need to know claim construction. You do need to have issues
15 of experts being involved a lot more to be able to really
16 hammer them out as opposed to just, here's the prior art,
17 here's what we have. I think that there's a distinction
18 between 112 issues and how fulsome they need to be at this
19 stage versus maybe the 102, 103.

20 THE COURT: All right. And then, lastly,
21 Mr. Pivovar, before I turn to the next issue, you see what
22 the plaintiff is requesting of you with regard to
23 supplementing your invalidity contentions before the
24 plaintiff is in turn required to make a final decision on
25 whether it's going to stick with its 36 now asserted claims

1 or whether it's going to alter that, and I think that's set
2 out on page 2 of the plaintiffs' letter.

3 If I was saying to you, if I had to decide
4 between whether to require you to do exactly what plaintiff
5 asked as to all 105 claims on that page, that could be one
6 outcome. Another outcome is that I just agree with you and
7 that what you've done is sufficient across the board.
8 That's the second.

9 Are those my choices or is there any point at
10 which you say, Judge, look. If you are thinking about
11 making us do anything more as to all 105, what you shouldn't
12 do is to require the entirety of what plaintiff asks? Look,
13 at a minimum, what we might be able to do without much
14 additional prejudice is blank by way of further
15 supplementation.

16 Is there any middle ground here or is it just
17 one or the other?

18 MR. PIVOVAR: I think, your Honor, the middle
19 ground seems -- I think probably the best way to proceed
20 would be to say, if the plaintiffs can actually show that
21 there is some form of prejudice down the road, that there's
22 some, like, new argument that they couldn't have seen or
23 that they couldn't have predicted and they couldn't have
24 built into their selection of claims, then maybe you would
25 consider whether that would be enough of a justification,

1 because I don't know that we could do anything at this
2 point that wouldn't be everything that they are asking for,
3 that they wouldn't be later complaining that we didn't do
4 enough.

5 So my concern would be that maybe there isn't
6 much middle ground that we could do that would satisfy what
7 they are actually asking for.

8 THE COURT: And if I were to do something like
9 that, to leave that out open, is there a reason why you then
10 wouldn't be in a position to supplement your invalidity
11 contentions as to the 36 claims that at least plaintiff has
12 currently selected?

13 MR. PIVOVAR: Your Honor, I believe that as part
14 of the schedule, we're supposed to select our 40 grounds
15 that are part of the schedule. It was our view that that
16 would be for those 36 specific claims.

17 THE COURT: Oh, that's right. When is that?

18 MR. PIVOVAR: My point being, that selection is
19 forthcoming.

20 THE COURT: I can't recall when the deadline is.
21 Do you know?

22 MR. PIVOVAR: I believe --

23 MS. PASCALE: Your Honor, it's December 18th.

24 THE COURT: All right. I see. Got it. Your
25 point is that process is already scheduled to happen in some

1 form.

2 Now, when you've selected those, selecting
3 references I suppose is one thing, but then supplementing
4 with the kind of detail that the plaintiff is asking for as
5 to the remaining claims is another. Is there any reason why
6 you shouldn't be required after you narrowed the references
7 to do that?

8 MR. PIVOVAR: Oh, you mean when we get through
9 the 40 grounds? Well, I think that there's going to be a
10 supplementation that's going to happen, and so we're going
11 to select the grounds and then we will supplement.

12 The question really is, your Honor: At what
13 point in time would it make sense for that to happen
14 considering all of the moving parts that we have? As part
15 of this as well, your Honor, if we're going to have to
16 select our prior art, we do have to get like what their
17 priority dates are in advance of that so they can help us,
18 but I think that has been resolved.

19 So the question is: At what point in time do we
20 do that? And I would suggest it makes the most sense to do
21 that after claim construction.

22 THE COURT: Okay. All right. Let me move on
23 here to the next issue, which is the response to
24 Interrogatory Number 1 as to the assertedly deficient
25 noninfringement contentions.

1 Mr. Altherr, let me let you add anything you
2 want to your argument there. Then I will follow up with a
3 question or two.

4 MR. ALTHERR: Well, your Honor, I think this
5 goes back to Judge Stark's order on this, is that basically,
6 this is a rebuttal contention on infringement. So we gave
7 them detailed charts. We should get as good as we gave.

8 And all they did, they listed down a whole bunch
9 of claim elements and then they said they were invalid
10 either under 112 or not infringed. You know, that does not
11 answer the noninfringement issue when they throw in all of
12 these 112 issues. And they should at least be able to
13 identify, you know, what they are saying is invalidity under
14 112 with respect to what particular claims and claim terms
15 and what limitations they're saying are not infringed.

16 All right. Now, they said that they need this
17 claim construction, but that's going back to the point that
18 they're basically saying, you can't ever answer a contention
19 interrogatory until you have your claim construction, and
20 that's just not the case, your Honor. I'm sure you are
21 aware of that.

22 THE COURT: Right.

23 MR. ALTHERR: They've pled noninfringement.
24 They should be able to give us the basis for that. That's
25 all we're asking for.

1 THE COURT: Okay. Mr. Pivovar, I mean, here,
2 look. It's one thing with Exhibit A, you know. I mean,
3 clearly, a lot of time and effort went into that document,
4 and albeit, I understand the plaintiffs' arguments about why
5 it's still deficient with regard to your invalidity
6 contentions. But the noninfringement contentions, I
7 mean, what's the assertion as to why that effort is
8 good enough?

9 MR. PIVOVAR: So, your Honor, one of the key
10 issues that I think is being glossed over is that we
11 incorporated by reference all of the noninfringement
12 positions that we adopted in the preliminary injunction
13 phase, and those are like the ones that carry most of the --
14 I mean, those disputes have not changed. They're there.
15 They know what they are. We've laid them all out. And
16 those percolate across a lot of the claims.

17 THE COURT: Mr. Pivovar, on that front, I think
18 you're talking about your response at the bottom of page 2
19 of the letter where you say, while the preliminary
20 injunction phase of the case only involved six claims, due
21 to the extensive overlap and shared limitations across the
22 105 asserted claims, HyperBranch's positions during the
23 preliminary area injunction phase apply across many claims.

24 Am I right there that what you are saying is,
25 look. As to the 105 claims, the positions we took as, the

1 more detailed positions we took as to the six claims at
2 issue earlier, there are many, many claims to which those
3 same positions, many, many other claims of the remaining 99
4 to which the same positions would apply. It's just a matter
5 of determining which position applies to which claim. Is
6 that right?

7 MR. PIVOVAR: It's very much that, your Honor.
8 And keep in mind, too, when we assert noninfringement of an
9 independent claim, then it applies to all of the dependent
10 claims. So one of the things that has happened in going
11 from the six from the preliminary injunction phase to the
12 105 here is that we had noninfringement arguments against
13 all of the independent claims that were asserted in the
14 preliminary injunction phase but one.

15 When they came back then and asserted 105 claims
16 where it was the independent claim, but then there's 12
17 dependent claims off of it, our noninfringement argument
18 still applies across all of them, and obviously plaintiffs
19 know this.

20 So that is another aspect of why they have,
21 like, all of our, the gist of our, like, proof for
22 noninfringement on the vast majority of the claims that span
23 the 105. That's just another added level as to why it works
24 out that you have noninfringement argument on one claim, but
25 actually applies across them.

1 THE COURT: Do you have any idea, for example,
2 as to how many dependent claims are tied up in the six
3 independent claims that we dealt with earlier?

4 MR. PIVOVAR: I think the vast bulk of them are.

5 THE COURT: Okay.

6 MR. PIVOVAR: Your Honor, for the most part,
7 there are only a couple of independent claims in the
8 patents, and there are a slew of dependent claims. So I
9 would say that, you know, if I was going to make sure --
10 their noninfringement arguments cover, they cover all of the
11 claims, and the gist is just a matter of whether, like, the
12 idea and the allegation is the same.

13 So, for instance, we had a big dispute about
14 whether Visualization, Inc. indicates a predetermined
15 fitness. And you may remember we talked about that for a
16 long time in the preliminary injunction phase.

17 THE COURT: Right.

18 MR. PIVOVAR: There are a couple of other
19 independent claims they've asserted that uses that exact
20 same language that might not have been implicated by the
21 preliminary injunction phase, but that language is exactly
22 the same, the arguments are exactly the same. That doesn't
23 change anything. So our noninfringement arguments apply
24 across all 105 claims that are presently asserted.

25 THE COURT: And if it's so that one could pretty

1 easily go back and take a look at each of these claims that
2 are currently being asserted and take a look at the specific
3 noninfringement arguments you made as to the six claims back
4 at the preliminary injunction phase and piece together,
5 okay, look. So for this claim number, you know, X, these
6 two arguments would apply clearly, and that we're making
7 those.

8 Why isn't it fair to make you do that? You are
9 the one responding to it. You've got that knowledge. Why
10 make the plaintiff try to figure out which of the many you
11 are citing as to claim number X? Why couldn't you do a
12 chart that at least puts that together and at least some way
13 that wouldn't be unduly prejudicial and would kind of
14 satisfy your responsibility?

15 MR. PIVOVAR: Your Honor, so that seems to be
16 more of a form over substance kind of response, which
17 obviously the form over substance we can deal with.

18 Like from a substantive perspective, we
19 obviously disclose all of this information that was there
20 and incorporated it into our responses, and if it's a matter
21 of just making a chart and then saying, you can see all of
22 these claim elements being argued here, I mean, that is
23 really just a question of form over substance, and we can
24 obviously transmit that form.

25 THE COURT: Well, I mean, I guess it's form over

1 substance if it's absolutely crystal clear exactly as to
2 each of the already asserted noninfringement arguments you
3 made, how they apply to each of the other claims at issue in
4 the case. If it's not absolutely a hundred percent crystal
5 clear, then it's not form over substance. Would you agree,
6 it would actually be kind of providing a response on a
7 claim-by-claim basis as to what your noninfringement
8 position is, wouldn't it?

9 MR. PIVOVAR: If that were the case, yes, but my
10 view is that I don't think there's a lot of debate over any
11 of the variability amongst the claims that might be there.
12 I mean, for the first part, the exact same language and
13 exact same arguments are going to apply for 75, 80 percent
14 of the claims at least. And I have not gone back and looked
15 at it. It might even be higher than that. And then like
16 the variability, it's the exact same language, just in a
17 different claim.

18 THE COURT: And for the dependent claims that
19 were not at issue in the earlier proceeding, is what you are
20 saying is, look, the reason why what we've said is
21 sufficient and the reason why it's sufficient just to refer
22 back to our positions at the preliminary injunction phase is
23 that we're not going to have any separate argument at this
24 stage as to why we don't infringe based on some unique
25 aspect of one of the dependent claims? It's all going to be

1 arguments that relate to what is contained within the
2 dependent claim because they're dependent on the independent
3 claims that we already addressed? Is that the position?

4 MR. PIVOVAR: Yes. At this point in time,
5 that's effectively where we're at.

6 THE COURT: Okay. Mr. Altherr, on your end, is
7 it the case that from the plaintiffs' perspective it's
8 crystal clear as to how the noninfringement positions the
9 defendant took as to the first six claims at issue in the
10 preliminary injunction phase apply to the 105 claims that
11 you currently had asserted?

12 MR. ALTHERR: Absolutely not, your Honor. For
13 example, their response to Interrogatory Number 1, when you
14 get to the substantive part where they are saying why they
15 don't infringe and say it's due to indefiniteness of
16 limitation. They go on and they list six pages,
17 double-spaced typed pages of claim limitations. All right?

18 Now, there weren't anywhere near that many
19 claim limitations at issue in the preliminary injunction
20 phase, so there's an awful lot of issues here that they are
21 raising that have nothing to do with the preliminary
22 injunction phase, were never even raised then, and are in
23 answer that respond to that interrogatory.

24 Additionally, as I said, your Honor, there are a
25 lot of these claims and it is not crystal clear exactly how

1 they are applying them. I understand what they did with
2 respect to the claims, the six claims that were at the
3 preliminary injunction phase. If they're not asserting any
4 other noninfringement defenses with respect to those other
5 than what was at the preliminary injunction phase, then for
6 those six claims, that's fine, but we do need to know what
7 their position is on what limitations are or are not being
8 practiced with respect to the remaining asserted claims.

9 THE COURT: Okay. Let me move on and ask you
10 about the remaining two issues. The first relates to
11 Interrogatory Number 3, and that's the interrogatory with
12 regard to substantial noninfringing uses for the accused
13 products. There I think the defendants' position is, "We
14 don't have to provide answers because the plaintiffs," and
15 I'm reading from page 3 of the defendants' responsive
16 letter, "have never made an assertion regarding
17 noninfringing uses."

18 So, in essence, I guess the assertion is have
19 not put at issue contributory infringement, at least that
20 piece of the requirements for contributory infringement in a
21 case.

22 What's your response to that assertion?

23 MR. ALTHERR: Your Honor, they basically asked
24 us to disprove all negatives. All right? We have made the
25 allegation that there is contributory infringement and that

1 there is no noninfringing use.

2 We asked them if they have a substantial
3 noninfringing use, if they contend that there is a
4 substantial noninfringing use, identify it for us.

5 THE COURT: And when you say you've made the
6 assertion, are you referring to the allegations in Count
7 4?

8 MR. ALTHERR: In --

9 THE COURT: The contributory infringement count
10 of your complaint?

11 MR. ALTHERR: Yes, your Honor.

12 THE COURT: Okay. So, you say, look, we put
13 contributory infringement at issue with regard to the
14 patents as they relate to the accused products. We've
15 asserted that there are no substantial noninfringing uses of
16 those products, and now we're asking to the extent the
17 defendant has a position otherwise, what is it? Is that
18 right?

19 MR. ALTHERR: Absolutely, your Honor.

20 THE COURT: Okay. Mr. Pivovar, why haven't the
21 plaintiffs sufficiently, quote, "put at issue" -- I mean, it
22 sounds like a repeat of the argument we just had as to your
23 dispute. But why haven't they specifically put at issue the
24 question as to whether there are noninfringing uses of the
25 products for contributory infringement purposes by making

1 the allegation in their complaint, and why shouldn't you
2 have to answer the interrogatory?

3 MR. PIVOVAR: All right. So infringement,
4 your Honor, as you well know, is performed on a
5 claim-by-claim basis just like invalidity. So if you are
6 going to say that there are no substantial noninfringing
7 uses, you have that on a claim-by-claim basis, because each
8 of the claims have different requirements and each of the
9 claims have potentially allegations that would have
10 different noninfringing uses.

11 We don't know what they're alleging with respect
12 to each of those claims, and they don't make an allegation
13 that there are no substantial noninfringing uses for each of
14 the claims that are asserted, and they don't provide any
15 factual detail regarding it. That said, your Honor, we did
16 say in our response like we said in the preliminary
17 injunction case, we don't actually infringe the claims, so
18 there can be no contributory infringement. And then it's
19 your burden to point out to us what you believe to be that
20 there are no non-substantial, or no substantial
21 noninfringing uses.

22 On a meet and confer I asked counsel to identify
23 for me in your contention where it is that you claim and
24 you assert in them that allegation that there are no
25 substantial noninfringing uses, and I've never had that

1 identified to me, and I wasn't able to find it in their
2 contentions.

3 THE COURT: Why isn't this the flip side of the
4 argument we were having with regard to your dispute? In
5 other words, I thought with regard to the invalidity
6 defense, you said, look, we put the defense at issue, so
7 it's fair game for each side to seek relevant discovery
8 about their contentions that in some way relate to the
9 defense. And so here, just like you could, you know, the
10 plaintiffs will claim, look, they've made the claim. They
11 made the claim of contributory infringement. They put the
12 claim at issue.

13 If you felt that you wanted more information,
14 you could, A, you could issue contention interrogatories
15 about this aspect of contributory infringement to them.
16 They could do it to you. If for some reason you thought the
17 complaint wasn't sufficiently specific in terms of its
18 allegations, you could have moved to dismiss or sought
19 amendment, but since the claim has been raised, discovery
20 about elements of the claim, or in your case the defense,
21 are, quote, "relevant." Why doesn't that same rationale
22 apply to this issue as well?

23 MR. PIVOVAR: Your Honor, I think that's
24 absolutely true, and the issue we have here is how much
25 level of detail did they give and what are they asking for

1 out of us.

2 Specifically, when you have like our responses
3 are commensurate with the level of detail that they've
4 given, they've said, you have no substantial noninfringing
5 uses. We've said, first of all, we don't infringe, and, by
6 the way, we do.

7 They have not given us any factually specific
8 allegations as to support their assertion that there are no
9 substantial noninfringing uses. It's their burden to do
10 that and do what they are saying about the other burden.
11 But different from what we've done in our invalidity
12 contentions, we've given detailed contentions on a
13 claim-by-claim basis that puts in dispute the priority
14 date of all of those claims because the references apply.
15 Here we don't have that on a claim-by-claim basis, your
16 Honor.

17 THE COURT: But wasn't part of your argument as
18 to the other issue, that wasn't even a factor? It wouldn't
19 even have mattered if you had put forward invalidity
20 contentions at this stage, because the contentions you were
21 seeking were already, quote, "relevant" because the defense
22 was at issue in the case. Right? I mean, that was your
23 lead argument on that issue. Right?

24 MR. PIVOVAR: No. Putting into dispute an issue
25 on which another party has the burden, it's typically one of

1 the -- and I think it's typically that you have to put it in
2 dispute first, which we did with the invalidity contention,
3 and then they have an allegation to respond.

4 The whole question is: What's the me, too? And
5 I think that's the main thrust and what we've obviously
6 contended regardless of anything else that's in dispute and
7 they have to respond to the invalidity contentions.

8 Now, here we don't have that level of detail
9 with regard to their allegations of contributory
10 infringement. They have their allegations of literal
11 infringement. We've said that we don't infringe. We've
12 laid out why. They don't give us the allegations of
13 contributory infringement on a claim-by-claim basis, which
14 is exactly what's required. So that's a little bit of the
15 distinction between, you know, what we've done with the
16 burden shifting on the invalidity front, what they have not
17 done with the burden shifting on the contributory
18 infringement front.

19 THE COURT: Okay. And then, lastly, as to the
20 last issue regarding Interrogator No. 8, Mr. Altherr, there,
21 I understand that as to that interrogatory, that the
22 defendant has asserted that it believes on the one hand that
23 there may be circumstances in which, for example, physicians
24 don't follow the instructions at issue and they've cited
25 some hypothetical situations where that could occur. You've

1 asked for their position as to what do they know.

2 Are there circumstances they are aware of in
3 which, say, for example, people that were listed in response
4 to Interrogatory No. 6 have not followed those instructions?
5 And what you are saying is, to the extent that defendant is
6 aware of such circumstances as opposed to hypotheticals,
7 they should at least be required to respond and articulate
8 what their knowledge is. Is that right?

9 MR. ALTHERR: Yes, your Honor. It goes a little
10 further than that. The interrogatory says that if they
11 intended to rely upon that they didn't follow the
12 instructions in order to avoid the inducement claim, that
13 they should tell us what that was that they didn't do. And
14 if they don't have anything that they can point to that they
15 intend to rely on, then they should say so.

16 THE COURT: Well, obviously, you would
17 acknowledge that like with any response, there can be
18 supplementation. So, for example, it may not be the case
19 sitting here that they have a firm sense as to every, even
20 as to every person listed in their response to the earlier
21 interrogatory as to whether or not they followed every
22 instruction as to every product. Right? I mean, that's
23 just what they're currently aware of?

24 MR. ALTHERR: Right. Your Honor, it's ones that
25 they intend to rely upon. All right? That we were asking

1 for.

2 THE COURT: Based on their current knowledge.

3 Right?

4 MR. ALTHERR: Absolutely. Based on their
5 current knowledge. And obviously, they could supplement if
6 they have something at this time. If they don't have
7 anything at this time, then they should say so.

8 THE COURT: Okay. And to the extent part of
9 their response to the interrogatory was that certain
10 information disclosed in the preliminary injunction phase of
11 the case indicates that individuals that have used the
12 products have done so in a manner that isn't consistent with
13 the instructions, is your response, well, look, what we were
14 asking for you, you know, not just to point vaguely to some
15 phase of the case, but tell us what you think falls into
16 that bucket?

17 MR. ALTHERR: Absolutely, your Honor. I have no
18 idea what information they are talking about.

19 THE COURT: All right. Mr. Pivovar, on this
20 front and maybe focusing on that particular aspect of your
21 response, it sounds like in terms of quote, "specific," the
22 defendant does have in its mind certain information from the
23 preliminary injunction stage that would constitute
24 circumstances where certain individuals have used the
25 products in a way not consistent with the instructions.

1 Why wouldn't it be fair for the defendant to be
2 required to at least set out what it knows and has frame of
3 mind on that front that it intends to point to by way of its
4 defenses?

5 MR. PIVOVAR: Your Honor, I think that the
6 defendants can glean that information from what they know
7 from the preliminary injunction phase. If you want, you
8 think it's necessary for us to tell them why we think that
9 people have utilized it, there are three doctors that use
10 it, and then there was also their expert as well as, you
11 know, expert, you know, to lay out all of those specific
12 things that are in the actual documents already and link it
13 up, we can do that.

14 THE COURT: Yes. I think I do, at a minimum, by
15 pointing to specific portions of the record or by providing
16 it in a narrative, because that's what's required by the
17 rules with regard to responses to discovery requests like
18 these.

19 But aside from those instances, is your
20 position, look. We can only respond by way of information
21 that we currently are aware of and intend to rely on, and it
22 could be the case as we go further that with regard to some
23 of the previously mentioned individuals or otherwise, we
24 obtain additional information about folks not following
25 instructions. If we learn that, we'll supplement and do it

1 timely, but otherwise the information we've already
2 discussed from the preliminary injunction phase is the sum
3 and substance of what we have to respond here.

4 Is that your position?

5 MR. PIVOVAR: It is, your Honor. And also
6 folded within that is our objection to the interrogatory
7 per se, because what they are asking us to do is to identify
8 not only the individuals who have used the product, but then
9 to assign to them the way that they didn't follow the
10 instructions, which is not something our client has done
11 over time.

12 They have a list of all of the people that we've
13 given them in response to the interrogatory that we know of
14 right now that have used the product, and then what we have
15 is an investigation that we did with the client saying, hey,
16 what do you remember about people not following the
17 directions? Let's go through all the directions and see if
18 there's anywhere you recall instances where people didn't
19 follow them, which is what they are asking for, and we've
20 done that. But we just don't have the capability to go back
21 and say, well, my client remembers at this given time with
22 this individual, he was the one who made the error.

23 So the problem we really have with this
24 interrogatory at one level, your Honor, is, like, we are
25 giving them the responses that we have to the level that

1 we'll be able to give it to them, but some of the
2 information is just information that we don't have.

3 THE COURT: Well, no. I understand your
4 objection as to breadth, for example, in that respect. But
5 those would be circumstances that you don't, quote, "intend
6 to rely on at least at this stage." Right? You can't rely
7 on as part of your case information that you are not aware
8 of because, I mean, fair enough?

9 MR. PIVOVAR: Well, so it's a different thing.
10 Right? We wouldn't say that any individual that is
11 identified had a specific instance where he didn't follow
12 the instructions, but the factual matter that people don't
13 always follow the instructions is absolutely one we're going
14 to rely on. Right? And we have facts that demonstrate
15 that.

16 How they've written their interrogatories,
17 they're trying to say, if you can't assign to an individual
18 an inability or a failure to follow an instruction, then you
19 don't get to bring it in, and that's really the issue we
20 have with this. We don't have the ability to link that up
21 doesn't mean it didn't happen.

22 THE COURT: All right.

23 MR. PIVOVAR: Right? So that's really the issue
24 that they're going for with that.

25 THE COURT: So I think I see what you are

1 saying. You are saying, look, we might well have testimony
2 at some point which we think is admissible testimony that
3 explains how, say, groups of people at large, you know,
4 are likely to not have followed certain instructions that
5 we think is relevant and admissible and that they object,
6 we'll explain why it is. But what we don't want, you know,
7 and we may separately have information about specific
8 individuals who have not followed the instructions in
9 specific ways, but even if we provide the latter, we don't
10 want to be precluded from arguing that the former kind of
11 evidence is perfectly good evidence that can come in at
12 trial. Is that the idea?

13 MR. PIVOVAR: Exactly. At this stage, and we
14 have not gone back and done all of the kind of, like you've
15 mentioned, supplemental aspects, are there any individuals
16 who have actually used it and whether that turns out to be
17 material to our case, or do we want to at some time in the
18 future go and find that out. We may very well.

19 THE COURT: Okay. All right. Well, thank you,
20 counsel. I appreciate the argument on these plaintiffs'
21 issues. Some of them interrelate to each other and they
22 relate to dates at issue in the schedule.

23 I want the opportunity to at least reflect for a
24 moment on what the parties have said in the call before
25 deciding them, so what I will do is, to do that and then

1 expect in the next short time, the next couple of days, to
2 issue a short order that resolves the plaintiffs' requests,
3 and to the extent it's necessary, sets out how those
4 requests should be responded to and the deadlines that will
5 be required for responses and how those deadlines will
6 relate to the current deadlines in the case that are
7 currently set.

8 With that said, is there anything further we
9 need to take up at this time from a procedural perspective
10 from the plaintiffs' side, Mr. Altherr?

11 MR. ALTHERR: No, your Honor.

12 THE COURT: Okay. And from the defendants'
13 side, Mr. Pivovar?

14 MR. PIVOVAR: Actually, your Honor, the
15 selection of art in the next step, and Ms. Pascale
16 identified, that's scheduled for December 18th. That's
17 actually a Sunday. Is there any chance we could get an
18 oral order for you to slide that out a day to the 19th,
19 please?

20 THE COURT: No problem. So I hadn't realized
21 that, and that's an easy one. We'll make, to the extent
22 that that date is on a Sunday, which Mr. Pivovar said it is,
23 we'll say that the current deadline is now not
24 December 18th, but December 19th, which I understand to be a
25 Monday.

1 MR. PIVOVAR: Excellent. Thank you, your Honor.

2 THE COURT: All right. Anything further?

3 MR. PIVOVAR: No, your Honor.

4 THE COURT: All right. Thank you to all
5 counsel. I appreciate it. And as I said, I will try to
6 resolve these remaining issues as soon as I can.

7 Everyone, I wish you a very good day and a good week.
8 Take care.

9 (Counsel respond, "Thank you, your Honor.")

10 THE COURT: All right.

11 (Telephone conference concluded at 3:15 p.m.)

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Exhibit 2

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

INTEGRA LIFESCIENCES CORP., INTEGRA
LIFESCIENCES SALES LLC, CONFLUENT
SURGICAL, INC., AND INCEPT LLC,

Plaintiffs,

v.

HYPERBRANCH MEDICAL TECHNOLOGY,
INC.,

Defendant.

C.A. No. 15-819-LPS-CJB

**PLAINTIFFS' SUPPLEMENTAL OBJECTIONS AND ANSWERS
TO HYPERBRANCH'S INTERROGATORIES NOS. 1 AND 2**

Pursuant to Rules 26 and 33 of the Federal Rules of Civil Procedure, the Local Rules for the U.S. District Court for the District of Delaware, and subject to their rights to supplement these objections later in discovery, Plaintiffs Integra LifeSciences Corp., Integra LifeSciences Sales LLC, Confluent Surgical, Inc., and Incept LLC (collectively "Plaintiffs," as well as "Integra," "Integra Sales," "Confluent," and "Incept," respectively) hereby provide the following supplemental objections and responses to Defendant HyperBranch Medical Technology's ("HyperBranch") First Set of Interrogatories (Nos. 1 and 2), including each and every definition, instruction, and interrogatory contained therein (collectively "HyperBranch's First Set of Interrogatories"). The fact that Plaintiffs provide an answer to an interrogatory does not constitute an admission or acknowledgement that the interrogatory is proper, that the answers sought are within the bounds of discovery, or that requests for similar information will be treated in a similar fashion. Plaintiffs do not waive any objection by producing such documents, things, or answers, and Plaintiffs reserve the right to continue investigating these matters, to supplement their objections, and to object to future discovery on the same or related matters. Plaintiffs

further reserve the right to object to the admissibility of any answer produced pursuant to these interrogatories, in whole or in part, on any ground including without limitation materiality, relevance, and privilege.

GENERAL OBJECTIONS

Plaintiffs incorporate by reference their General Objections and Objections to Specific Definitions to HyperBranch's Requests for Production. Each of these General Objections is incorporated into the specific objections set forth below, whether or not separately set forth therein.

1. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it seeks to impose upon Plaintiffs any obligation or responsibility broader than, different from, or in addition to those obligations and requirements mandated by the Federal Rules of Civil Procedure, the Federal Rules of Evidence (collectively, the "Federal Rules"), and the Local Rules for the United States District Court for the District of Delaware (the "Local Rules").

2. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs do not intend to produce such privileged or protected documents or information. To the extent that any document or information which is properly subject to any such privilege or protection is inadvertently produced in connection with an answer to an interrogatory, such inadvertent disclosure is not to be construed as a waiver of such privilege or protection, and such document and information, and all copies thereof, shall be returned to counsel for Plaintiffs, in accordance with Fed. R. Evid. 502(b), Fed. R. Civ. P. 26(b)(5)(B), and any relevant Order entered by the Court. Further,

Plaintiffs will limit their privilege log to pre-lawsuit privileged or protected documents or information, if any exist.

3. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent they contain misstatements of fact and/or inaccurate assumptions. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it is overly broad, unduly burdensome, or oppressive. Plaintiffs further object to each and every definition, instruction, and interrogatory to the extent it calls for information that is irrelevant to any claim or defense in this action.

4. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it seeks information already in the possession, custody, or control of HyperBranch as being overly broad, unduly burdensome, expensive, and inconsistent with the Federal Rules.

5. Plaintiffs object to each and every definition, instruction, and interrogatory as being unduly burdensome to the extent it seeks facts, documents, and/or information that is publicly available, unreasonably cumulative or duplicative, or already known and equally available to HyperBranch.

6. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it is vague, ambiguous, fails to describe the information sought with the required reasonable particularity, or is so unintelligible that Plaintiffs cannot ascertain what information is responsive.

7. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it seeks to impose upon Plaintiffs an obligation to investigate or discover information, materials, or documents from any entity other than Plaintiffs, including, but not limited to, third parties or non-parties.

8. Plaintiffs' agreement to furnish information in response to HyperBranch's Interrogatories shall not be deemed to constitute an admission as to its relevancy, nor is it intended to waive any right to object to its admissibility at trial.

9. Plaintiffs object to each interrogatory that requests "each," "every," or "all" (and to similar overly broad terms) information or documents as overbroad and unduly burdensome. Plaintiffs will undertake a diligent and reasonable investigation to gather information in their possession, custody, or control that is responsive to the non-objectionable portions of each interrogatory.

10. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it contains subparts, is compound and conjunctive, and is otherwise inconsistent with or exceeds the number of interrogatories permitted by any relevant Order entered by the Court. The Court has set a limit of 25 interrogatories for each side. In answering any or all of these Interrogatories or subparts, Plaintiffs do so without waiver of their right to object to and refuse to answer any future Interrogatories on the grounds that such Interrogatories are in excess of the number permitted by the Federal and Local Rules and the Court's Scheduling Order.

11. In addition to these General Objections, Plaintiffs have specific objections as set forth below. By stating these specific objections, Plaintiffs do not waive any of the General Objections that may also be applicable to specific interrogatories.

OBJECTIONS TO SPECIFIC DEFINITIONS

1. Plaintiffs object to the definition of the terms "Plaintiffs," "You," and "Yours" to the extent those terms are overly broad and purport to require Plaintiffs to provide information and/or documents that are not currently within their possession, custody, or control. Plaintiffs object to the definitions of the terms "Plaintiffs," "You," and "Yours" as seeking the disclosure

of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law, in that the definitions specifically cover “attorneys.”

2. Plaintiffs object to the definition of “Accused Products” as overbroad, unduly burdensome, and irrelevant to any issue in this matter as “any and all products, activities, services, processes, systems, apparatuses, or things that Plaintiffs accuse of infringing the Asserted Patents in this Action, including Adherus Autospray Dural Sealant, Adherus Dural Sealant, and Adherus Spinal Sealant” include information, products, and/or documents that are not currently within the possession, custody, or control of Plaintiffs. Indeed, this definition explicitly includes documents and things which are in the exclusive control of Defendant and Third Parties.

3. Plaintiffs object to the definition of the term “each” to the extent that the definition purports to impose a meaning broader than the definition provided in the Federal Rules.

4. Plaintiffs object to the definition of “Prior Art” as overbroad, unduly burdensome, and irrelevant to any issue in this matter as “all things, patents, publications, disclosures, sales, or other acts or occurrences included within the broadest meaning of 35 U.S.C. § 102 (or any subpart thereof) and 35 U.S.C. § 103” and “publications, patents, patent applications, inventions by others, uses, sales or offers for sale, and disclosures” purports to require Plaintiffs to provide information and/or documents that are not currently within their possession, custody, or control.

OBJECTIONS AND ANSWERS TO SPECIFIC INTERROGATORIES

INTERROGATORY NO. 1 [9]. On a claim-by-claim basis for each and every claim of the Asserted Patents, identify each individual who You contend contributed to the conception of the invention set forth in each claim, including all supporting facts and evidence of the contribution to the conception of each claim by the identified individual(s) and the dates of such contribution(s).

OBJECTION AND ANSWER TO INTERROGATORY NO. 1 [9]:

Plaintiffs incorporate their General Objections and Objections to Specific Definitions by reference. Plaintiffs object to this interrogatory to the extent it purports to be a single interrogatory as it contains multiple and distinct subparts. Plaintiffs further object to this interrogatory to the extent it purports to be HyperBranch's first interrogatory. HyperBranch previously served Interrogatory Nos. 1-6 on October 23, 2015, and Interrogatory Nos. 7-8 on December 9, 2015. Thus, this interrogatory is HyperBranch's ninth interrogatory. Plaintiffs further object to this interrogatory as being unreasonably cumulative or duplicative, or already known to HyperBranch. *See* Interrogatory No. 1 served by HyperBranch on October 23, 2015. Plaintiffs further object to this interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs further object to the interrogatory as overbroad and unduly burdensome in that it requests identification of "all supporting facts and evidence of the contribution to the conception of each claim." Plaintiffs further object to this interrogatory as premature and irrelevant to the extent it is a contention interrogatory that seeks to impose a burden on Plaintiffs to provide a rebuttal position on conception of the inventions claimed in the patents-in-suit prior to the provision of any contention of invalidity of the claims that Defendant is required to provide on November 4, 2016. Validity, including validity of conception and proper inventorship is presumed by the issuance of the patent. Defendant bears the burden of establishing through its

invalidity contentions that there is an issue as to validity that would require Plaintiffs to prove an earlier date of invention or confirm the contribution of a listed inventor to the claims of the patents-in-suit. To date, Defendants validity contentions have not met that burden. Plaintiffs also object to this interrogatory to the extent it calls for legal argument and/or expert testimony, which Plaintiffs may provide, in due course and in accordance with the Court's Scheduling Order.

Subject to and without waiving its objections, Plaintiffs incorporate by reference their response to Interrogatory No. 1 served on November 13, 2015 and all supplements thereto and the Rebuttal Expert Report of Dr. Jimmy Mays and further respond that based on present information Chandrashekhar P. Pathak, Amarpreet S. Sawhney, and Peter G. Edelman contributed to the conception of one or more claims of the '034 Patent, the '406 Patent, the '5,705 Patent, the '566 Patent and the '418 Patent. Plaintiffs further respond that based on present information Amarpreet S. Sawhney, Steven Bennett, and Peter G. Edelman contributed to the conception of one or more claims of the '3,705 Patent. Defendants' present invalidity contentions do not place in dispute the conception or the named inventor's individual contributions to conception of any of the claims. Accordingly, Plaintiffs presently intend to rely on the effective filing date for each of patents-in-suit (including those patents and patent applications to which priority is claimed), including any evidence presented during prosecution of the patents-in-suit (including those patents and patent applications to which priority is claimed), the recitation of the named inventors on the face of each of the patents-in-suit, and the prior sworn deposition testimony (including exhibits used in those depositions) in this matter of the named inventors to identify the dates and individuals contributing to the conception of each of the claims of the patents-in-suit and the prior sworn testimony and multiple expert reports,

rebuttal expert reports, and/or declarations of Dr. Jimmy Mays that have previously been provided in this matter. Plaintiffs further respond that they have produced non-privileged documents pursuant to Federal Rule of Civil Procedure 33(d) (including the patents-in-suit, the patents and applications from which the patents-in-suit claim priority, the prosecution histories of these patents and patent applications, and the laboratory notebooks and the reports summarizing the laboratory work and notebooks of the inventors and individuals working under their direction (*See, e.g.*, Experimental Reports or Technical Documents having an ER[####] or TD-[####] identification)) from which HyperBranch may derive or ascertain information responsive to this interrogatory. Investigation of the facts is ongoing and Plaintiffs reserve the right to supplement this response to identify additional information and/or documents as more facts arise in discovery or as Defendant's invalidity contentions are fully and completely provided, in accordance with the Rules.

SUPPLEMENTAL OBJECTION AND ANSWER TO INTERROGATORY NO. 1[9]:

Subject to and without waiving any of its objections, based on information currently available to Plaintiffs and further to the Court's Order during the telephone conference on December 1, 2016, Plaintiffs supplement their previous response by stating that to the extent that Plaintiffs understand this interrogatory, Plaintiffs identify the following individuals who Plaintiffs currently contend to have contributed to the conception of the inventions set forth in the Asserted Claims and Plaintiffs contentions as to the date of conception of the inventions set forth in the Asserted Claims (to the extent that the "Earlier Conception Date" column is blank for any respective row, in the following tables, Plaintiffs are currently relying on the "Earlier Effective Filing Date" as also the "Earlier Conception Date"):

U.S. Patent 7,009,034

Claim	Earlier Effective Filing Dates	Earlier Conception Date*	Inventors
1	December 4, 1998 and December 3, 1999		Pathak
3	December 4, 1998 and December 3, 1999		Pathak
4	December 4, 1998 and December 3, 1999		Pathak
5	December 4, 1998 and December 3, 1999		Pathak
6	November 9, 2001	February 2001	Pathak, Sawhney, Edelman
9	December 4, 1998 and December 3, 1999		Pathak
10	November 9, 2001		Pathak, Sawhney, Edelman
11	December 4, 1998 and December 3, 1999		Pathak
12	December 4, 1998 and December 3, 1999		Pathak
13	December 4, 1998 and December 3, 1999		Pathak
14	December 3, 1999		Pathak
15	December 4, 1998 and December 3, 1999		Pathak
16	December 4, 1998 and December 3, 1999		Pathak
17	December 3, 1999		Pathak
18	December 4, 1998 and December 3, 1999		Pathak
19	December 4, 1998 and December 3, 1999		Pathak
20	December 4, 1998 and December 3, 1999		Pathak
21	December 4, 1998 and December 3, 1999		Pathak

U.S. Patent No. 7,332,566

Claim	Earlier Effective Filing Dates	Earlier Conception Date	Inventors
1	December 4, 1998 and December 3, 1999		Pathak
3	November 9, 2001	February 2001	Pathak, Sawhney, Edelman

4	December 4, 1998 and December 3, 1999		Pathak
6	December 4, 1998 and December 3, 1999		Pathak
7	November 9, 2001		Pathak, Sawhney, Edelman
8	December 4, 1998 and December 3, 1999		Pathak
9	November 9, 2001		Pathak, Sawhney, Edelman
10	December 3, 1999		Pathak
11	December 4, 1998 and December 3, 1999		Pathak
12	December 4, 1998 and December 3, 1999		Pathak
14	December 4, 1998 and December 3, 1999		Pathak
15	November 9, 2001		Pathak, Sawhney, Edelman
16	December 4, 1998 and December 3, 1999		Pathak
18	December 4, 1998 and December 3, 1999		Pathak
19	November 9, 2001		Pathak, Sawhney, Edelman
20	December 4, 1998 and December 3, 1999		Pathak
21	December 4, 1998 and December 3, 1999		Pathak
22	December 4, 1998 and December 3, 1999		Pathak
23	November 9, 2001		Pathak, Sawhney, Edelman
24	December 4, 1998 and December 3, 1999		Pathak
25	December 4, 1998 and December 3, 1999		Pathak
27	November 9, 2001	February 2001	Pathak, Sawhney, Edelman
28	December 4, 1998 and December 3, 1999		Pathak
30	December 4, 1998 and December 3, 1999		Pathak
31	November 9, 2001		Pathak, Sawhney, Edelman
32	December 3, 1999		Pathak

33	December 4, 1998 and December 3, 1999		Pathak
34	November 9, 2001		Pathak, Sawhney, Edelman
35	December 4, 1998 and December 3, 1999		Pathak
36	December 4, 1998 and December 3, 1999		Pathak
37	December 4, 1998 and December 3, 1999		Pathak
38	November 9, 2001		Pathak, Sawhney, Edelman

U.S. Patent No. 7,592,418

Claim	Earlier Effective Filing Dates	Conception Date	Inventors
1	December 4, 1998 and December 3, 1999		Pathak
3	December 4, 1998 and December 3, 1999		Pathak
4	November 9, 2001	February 2001	Pathak, Sawhney, Edelman
5	December 4, 1998 and December 3, 1999		Pathak
6	December 4, 1998 and December 3, 1999		Pathak
7	November 9, 2001		Pathak, Sawhney, Edelman
8	December 3, 1999		Pathak
9	December 4, 1998 and December 3, 1999		Pathak
10	November 9, 2001		Pathak, Sawhney, Edelman
11	December 4, 1998 and December 3, 1999		Pathak
13	December 4, 1998 and December 3, 1999		Pathak
14	December 4, 1998 and December 3, 1999		Pathak
15	December 4, 1998 and December 3, 1999		Pathak
16	December 4, 1998 and December 3, 1999		Pathak
22	December 4, 1998 and December 3, 1999		Pathak

23	December 4, 1998 and December 3, 1999		Pathak
24	December 4, 1998 and December 3, 1999		Pathak
25	December 4, 1998 and December 3, 1999		Pathak
26	November 9, 2001		Pathak, Sawhney, Edelman
27	December 4, 1998 and December 3, 1999		Pathak
28	December 4, 1998 and December 3, 1999		Pathak
29	December 4, 1998 and December 3, 1999		Pathak
30	November 9, 2001		Pathak, Sawhney, Edelman

U.S. Patent No. 6,566,406

Claim	Earlier Effective Filing Dates	Conception Dates	Inventors
1	December 4, 1998		Pathak
2	December 4, 1998		Pathak
6	December 4, 1998		Pathak
7	December 4, 1998		Pathak
8	December 4, 1998		Pathak
10	December 4, 1998		Pathak
12	December 4, 1998		Pathak
14	December 3, 1999		Pathak, Sawhney, Edelman
15	December 3, 1999		Pathak, Sawhney, Edelman
16	December 4, 1998		Pathak
19	December 4, 1998		Pathak
21	December 4, 1998		Pathak
23	December 3, 1999		Pathak, Sawhney, Edelman
24	December 3, 1999		Pathak, Sawhney, Edelman
25	December 3, 1999		Pathak, Sawhney, Edelman

U.S. Patent No. 8,003,705

Claim	Earlier Effective Filing Dates	Conception Dates	Inventors
1	May 28, 2008	December 2000	Sawhney, Bennett, Edelman
4	November 9, 2001		Sawhney, Edelman
5	November 9, 2001		Sawhney, Edelman
6	November 9, 2001		Sawhney, Edelman
11	November 9, 2001		Sawhney, Edelman
12	November 9, 2001		Sawhney, Edelman
13	November 9, 2001		Sawhney, Edelman
16	May 28, 2008	December 2000	Sawhney, Bennett, Edelman
19	May 28, 2008	December 2000	Sawhney, Bennett, Edelman

U.S. Patent No. 8,535,705

Claim	Earlier Effective Filing Dates	Conception Dates	Inventors
1	December 4, 1998 and December 3, 1999		Pathak
5	December 4, 1998 and December 3, 1999		Pathak
6	December 4, 1998 and December 3, 1999		Pathak
7	December 4, 1998 and December 3, 1999		Pathak
9	December 3, 1999		Pathak, Sawhney, Edelman
12	December 4, 1998 and December 3, 1999		Pathak
15	December 4, 1998 and December 3, 1999		Pathak
17	December 4, 1998 and December 3, 1999		Pathak

Plaintiffs reserve the right to amend or supplement this response as this case proceeds.

INTERROGATORY NO. 2 [10]. On a claim-by-claim basis for each and every claim of the Asserted Patents, identify what You contend to be the effective filing date for the claim, including all supporting facts and evidence for the identified effective filing date such as, without limitation, the specific page and lines of any prior filed applications that you contend supports Your identified effective filing date for each claim.

OBJECTION AND ANSWER TO INTERROGATORY NO. 2 [10]:

Plaintiffs incorporate their General Objections and Objections to Specific Definitions by reference. Plaintiffs object to this interrogatory to the extent it purports to be a single interrogatory as it contains multiple and distinct subparts. Plaintiffs further object to this interrogatory to the extent it purports to be HyperBranch's second interrogatory. HyperBranch previously served Interrogatory Nos. 1-6 on October 23, 2015, and Interrogatory Nos. 7-8 on December 9, 2015. Thus, this interrogatory is HyperBranch's tenth interrogatory. Plaintiffs further object to this interrogatory as being unreasonably cumulative or duplicative, or already known to HyperBranch. *See* Plaintiffs' Responses and Supplemental Responses to Interrogatory Nos. 1 and 8 and Rebuttal Expert Report of Dr. Jimmy Mays, hereby incorporated by reference in their entirety. Plaintiffs further object to this interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs further object to the interrogatory as overbroad and unduly burdensome and premature at this stage of the litigation in that it requests identification of "all of the factual and legal bases for that contention, and identify all documents and evidence you claim supports that contention." .” Plaintiffs further object to this interrogatory as premature and irrelevant to the extent it is a contention interrogatory that seeks to impose a burden on Plaintiffs to provide a rebuttal position on the effective filing date of each claim prior to the disclosure of any invalidity contention by the Defendant that puts at issue the effective filing date of any claim on which Defendant has the burden of proof and is required to provide its full and complete invalidity contentions. Validity of the claims is presumed by the issuance of the patent. Defendant bears the burden of establishing through its invalidity contentions that there is an issue

as to validity that would require Plaintiffs to prove an earlier effective filing date. To date, Defendants validity contentions have not met that burden. Plaintiffs further object to this Interrogatory to the extent it contains subparts which, together with the other Interrogatories, exceed the limit under the Federal Rules. Plaintiffs also object to this interrogatory to the extent it calls for legal argument and/or expert testimony, which Plaintiffs may provide, in due course and in accordance with the Court's Scheduling Order.

Subject to and without waiving its objections, Plaintiffs rely on the disclosures provided in the patents-in-suit including the related U.S. applications provided on the front of each of the patents in suit to provide an effective filing date for each of the claims. Particularly, the related U.S. applications listed on the face of the patents-in-suit show that the effective filing date for many of the limitations found in the claims of the patents-in-suit may extend back to at least as early as December 4, 1998 and possibly as early as September 23, 1996. For example, many of the limitations claimed in the patents-in-suit can expressly be found in the text of the related U.S. applications. (*See, e.g.*, visualization agent, precursors, biodegradable polymers, biodegradable polymeric crosslinkers, nucleophilic functional groups, electrophilic functional groups, hydrogel film thickness, and many others). Plaintiffs further respond that they have produced non-privileged documents pursuant to Federal Rule of Civil Procedure 33(d) for which the burden of deriving or ascertaining the answer will be substantially the same for HyperBranch as it is for plaintiffs, namely the patents-in-suit, the patents and applications from which the patents-in-suit claim priority, and prosecution histories of these patents and patent applications.

Plaintiffs also identify Exhibits 57 and 58 to the previous deposition of the inventors along with the transcripts of those depositions (i.e., Amar Sawhney and Steven Bennett) as providing

further information related to the effective filing date of the claims of the patents-in-suit. *See, e.g.,* Steve Bennett deposition transcript at pp. 147-48.

Investigation of the facts is ongoing and Plaintiffs reserve the right to supplement this response to identify additional information and/or documents as more facts arise in discovery and as rebuttal if Defendant meets its burden of setting forth a preliminary contention of invalidity that puts at issue the effective filing date of one or more claims of the patents-in-suit in accordance with the rules and the Scheduling Order in this matter.

SUPPLEMENTAL OBJECTION AND ANSWER TO INTERROGATORY NO. 2[10]:

Subject to and without waiving any of its objections, based on information currently available to Plaintiffs, Plaintiffs supplement their previous response by stating that to the extent that Plaintiffs understand this interrogatory, Plaintiffs incorporate by reference their response to Interrogatory No. 1[9] and all supplements thereto as identifying Plaintiffs current contentions as to the effective filing dates earlier than the filing date of the application that directly issued as the U.S. Patent and supporting evidence for the inventions set forth in the Asserted Claims. Plaintiffs reserve the right to amend or supplement this response as this case proceeds.

AS TO OBJECTIONS ONLY:

DATED: December 9, 2016

/s/ Karen L. Pascale
An Attorney for Plaintiffs, Integra LifeSciences Corp., Integra LifeSciences Sales LLC, Confluent Surgical, Inc., and Incept LLC

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(Continued . . .)

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CERTIFICATE OF SERVICE

I, Karen L. Pascale, Esquire, hereby certify that on December 9, 2016, I caused true and correct copies of the foregoing document to be served upon the following counsel of record by e-mail:

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*Attorneys for Plaintiffs Integra LifeSciences Corp.,
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Inc., and Incept LLC*

Exhibit 3

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

INTEGRA LIFESCIENCES CORP., INTEGRA
LIFESCIENCES SALES LLC, CONFLUENT
SURGICAL, INC., AND INCEPT LLC,

Plaintiffs,

v.

HYPERBRANCH MEDICAL TECHNOLOGY,
INC.,

Defendant.

C.A. No. 15-819-LPS-CJB

PLAINTIFFS' OBJECTIONS AND ANSWERS
TO HYPERBRANCH'S FIRST SET OF INTERROGATORIES (NOS. 1-7)

Pursuant to Rules 26 and 33 of the Federal Rules of Civil Procedure, the Local Rules for the U.S. District Court for the District of Delaware, and subject to their rights to supplement these objections later in discovery, Plaintiffs Integra LifeSciences Corp., Integra LifeSciences Sales LLC, Confluent Surgical, Inc., and Incept LLC (collectively "Plaintiffs," as well as "Integra," "Integra Sales," "Confluent," and "Incept," respectively) hereby object to Defendant HyperBranch Medical Technology's ("HyperBranch") First Set of Interrogatories served on September 23, 2016, including each and every definition, instruction, and interrogatory contained therein (collectively "HyperBranch's First Set of Interrogatories"). The fact that Plaintiffs provide an answer to an interrogatory does not constitute an admission or acknowledgement that the interrogatory is proper, that the answers sought are within the bounds of discovery, or that requests for similar information will be treated in a similar fashion. Plaintiffs do not waive any objection by producing such documents, things, or answers, and Plaintiffs reserve the right to continue investigating these matters, to supplement their objections, and to object to future discovery on the same or related matters. Plaintiffs further reserve the

right to object to the admissibility of any answer produced pursuant to these interrogatories, in whole or in part, on any ground including without limitation materiality, relevance, and privilege.

GENERAL OBJECTIONS

Plaintiffs incorporate by reference their General Objections and Objections to Specific Definitions to HyperBranch's Requests for Production. Each of these General Objections is incorporated into the specific objections set forth below, whether or not separately set forth therein.

1. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it seeks to impose upon Plaintiffs any obligation or responsibility broader than, different from, or in addition to those obligations and requirements mandated by the Federal Rules of Civil Procedure, the Federal Rules of Evidence (collectively, the "Federal Rules"), and the Local Rules for the United States District Court for the District of Delaware (the "Local Rules").

2. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs do not intend to produce such privileged or protected documents or information. To the extent that any document or information which is properly subject to any such privilege or protection is inadvertently produced in connection with an answer to an interrogatory, such inadvertent disclosure is not to be construed as a waiver of such privilege or protection, and such document and information, and all copies thereof, shall be returned to counsel for Plaintiffs, in accordance with Fed. R. Evid. 502(b), Fed. R. Civ. P. 26(b)(5)(B), and any relevant Order entered by the Court. Further,

Plaintiffs will limit their privilege log to pre-lawsuit privileged or protected documents or information, if any exist.

3. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent they contain misstatements of fact and/or inaccurate assumptions. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it is overly broad, unduly burdensome, or oppressive. Plaintiffs further object to each and every definition, instruction, and interrogatory to the extent it calls for information that is irrelevant to any claim or defense in this action.

4. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it seeks information already in the possession, custody, or control of HyperBranch as being overly broad, unduly burdensome, expensive, and inconsistent with the Federal Rules.

5. Plaintiffs object to each and every definition, instruction, and interrogatory as being unduly burdensome to the extent it seeks facts, documents, and/or information that is publicly available, unreasonably cumulative or duplicative, or already known and equally available to HyperBranch.

6. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it is vague, ambiguous, fails to describe the information sought with the required reasonable particularity, or is so unintelligible that Plaintiffs cannot ascertain what information is responsive.

7. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it seeks to impose upon Plaintiffs an obligation to investigate or discover information, materials, or documents from any entity other than Plaintiffs, including, but not limited to, third parties or non-parties.

8. Plaintiffs' agreement to furnish information in response to HyperBranch's Interrogatories shall not be deemed to constitute an admission as to its relevancy, nor is it intended to waive any right to object to its admissibility at trial.

9. Plaintiffs object to each interrogatory that requests "each," "every," or "all" (and to similar overly broad terms) information or documents as overbroad and unduly burdensome. Plaintiffs will undertake a diligent and reasonable investigation to gather information in their possession, custody, or control that is responsive to the non-objectionable portions of each interrogatory.

10. Plaintiffs object to each and every definition, instruction, and interrogatory to the extent it contains subparts, is compound and conjunctive, and is otherwise inconsistent with or exceeds the number of interrogatories permitted by any relevant Order entered by the Court. The Court has set a limit of 25 interrogatories for each side. In answering any or all of these Interrogatories or subparts, Plaintiffs do so without waiver of their right to object to and refuse to answer any future Interrogatories on the grounds that such Interrogatories are in excess of the number permitted by the Federal and Local Rules and the Court's Scheduling Order.

11. In addition to these General Objections, Plaintiffs have specific objections as set forth below. By stating these specific objections, Plaintiffs do not waive any of the General Objections that may also be applicable to specific interrogatories.

OBJECTIONS TO SPECIFIC DEFINITIONS

1. Plaintiffs object to the definition of the terms "Plaintiffs," "You," and "Yours" to the extent those terms are overly broad and purport to require Plaintiffs to provide information and/or documents that are not currently within their possession, custody, or control. Plaintiffs object to the definitions of the terms "Plaintiffs," "You," and "Yours" as seeking the disclosure

of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law, in that the definitions specifically cover “attorneys.”

2. Plaintiffs object to the definition of “Accused Products” as overbroad, unduly burdensome, and irrelevant to any issue in this matter as “any and all products, activities, services, processes, systems, apparatuses, or things that Plaintiffs accuse of infringing the Asserted Patents in this Action, including Adherus Autospray Dural Sealant, Adherus Dural Sealant, and Adherus Spinal Sealant” include information, products, and/or documents that are not currently within the possession, custody, or control of Plaintiffs. Indeed, this definition explicitly includes documents and things which are in the exclusive control of Defendant and Third Parties.

3. Plaintiffs object to the definition of the term “each” to the extent that the definition purports to impose a meaning broader than the definition provided in the Federal Rules.

4. Plaintiffs object to the definition of “Prior Art” as overbroad, unduly burdensome, and irrelevant to any issue in this matter as “all things, patents, publications, disclosures, sales, or other acts or occurrences included within the broadest meaning of 35 U.S.C. § 102 (or any subpart thereof) and 35 U.S.C. § 103” and “publications, patents, patent applications, inventions by others, uses, sales or offers for sale, and disclosures” purports to require Plaintiffs to provide information and/or documents that are not currently within their possession, custody, or control.

OBJECTIONS AND ANSWERS TO SPECIFIC INTERROGATORIES

INTERROGATORY NO. 1 [9]. On a claim-by-claim basis for each and every claim of the Asserted Patents, identify each individual who You contend contributed to the conception of the invention set forth in each claim, including all supporting facts and evidence of the contribution to the conception of each claim by the identified individual(s) and the dates of such contribution(s).

01:19460568.1

OBJECTION AND ANSWER TO INTERROGATORY NO. 1 [9]:

Plaintiffs incorporate their General Objections and Objections to Specific Definitions by reference. Plaintiffs object to this interrogatory to the extent it purports to be a single interrogatory as it contains multiple and distinct subparts. Plaintiffs further object to this interrogatory to the extent it purports to be HyperBranch's first interrogatory. HyperBranch previously served Interrogatory Nos. 1-6 on October 23, 2015, and Interrogatory Nos. 7-8 on December 9, 2015. Thus, this interrogatory is HyperBranch's ninth interrogatory. Plaintiffs further object to this interrogatory as being unreasonably cumulative or duplicative, or already known to HyperBranch. *See* Interrogatory No. 1 served by HyperBranch on October 23, 2015. Plaintiffs further object to this interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs further object to the interrogatory as overbroad and unduly burdensome in that it requests identification of "all supporting facts and evidence of the contribution to the conception of each claim." Plaintiffs further object to this interrogatory as premature and irrelevant to the extent it is a contention interrogatory that seeks to impose a burden on Plaintiffs to provide a rebuttal position on conception of the inventions claimed in the patents-in-suit prior to the provision of any contention of invalidity of the claims that Defendant is required to provide on November 4, 2016. Validity, including validity of conception and proper inventorship is presumed by the issuance of the patent. Defendant bears the burden of establishing through its invalidity contentions that there is an issue as to validity that would require Plaintiffs to prove an earlier date of invention or confirm the contribution of a listed inventor to the claims of the patents-in-suit. To date, Defendants validity contentions have not met that burden. Plaintiffs

also object to this interrogatory to the extent it calls for legal argument and/or expert testimony, which Plaintiffs may provide, in due course and in accordance with the Court's Scheduling Order.

Subject to and without waiving its objections, Plaintiffs incorporate by reference their response to Interrogatory No. 1 served on November 13, 2015 and all supplements thereto and the Rebuttal Expert Report of Dr. Jimmy Mays and further respond that based on present information Chandrashekhar P. Pathak, Amarpreet S. Sawhney, and Peter G. Edelman contributed to the conception of one or more claims of the '034 Patent, the '406 Patent, the '5,705 Patent, the '566 Patent and the '418 Patent. Plaintiffs further respond that based on present information Amarpreet S. Sawhney, Steven Bennett, and Peter G. Edelman contributed to the conception of one or more claims of the '3,705 Patent. Defendants' present invalidity contentions do not place in dispute the conception or the named inventor's individual contributions to conception of any of the claims. Accordingly, Plaintiffs presently intend to rely on the effective filing date for each of patents-in-suit (including those patents and patent applications to which priority is claimed), including any evidence presented during prosecution of the patents-in-suit (including those patents and patent applications to which priority is claimed), the recitation of the named inventors on the face of each of the patents-in-suit, and the prior sworn deposition testimony (including exhibits used in those depositions) in this matter of the named inventors to identify the dates and individuals contributing to the conception of each of the claims of the patents-in-suit and the prior sworn testimony and multiple expert reports, rebuttal expert reports, and/or declarations of Dr. Jimmy Mays that have previously been provided in this matter. Plaintiffs further respond that they have produced non-privileged documents pursuant to Federal Rule of Civil Procedure 33(d) (including the patents-in-suit, the

patents and applications from which the patents-in-suit claim priority, the prosecution histories of these patents and patent applications, and the laboratory notebooks and the reports summarizing the laboratory work and notebooks of the inventors and individuals working under their direction (*See, e.g.*, Experimental Reports or Technical Documents having an ER[####] or TD-[####] identification)) from which HyperBranch may derive or ascertain information responsive to this interrogatory. Investigation of the facts is ongoing and Plaintiffs reserve the right to supplement this response to identify additional information and/or documents as more facts arise in discovery or as Defendant's invalidity contentions are fully and completely provided, in accordance with the Rules.

INTERROGATORY NO. 2 [10]. On a claim-by-claim basis for each and every claim of the Asserted Patents, identify what You contend to be the effective filing date for the claim, including all supporting facts and evidence for the identified effective filing date such as, without limitation, the specific page and lines of any prior filed applications that you contend supports Your identified effective filing date for each claim.

OBJECTION AND ANSWER TO INTERROGATORY NO. 2 [10]:

Plaintiffs incorporate their General Objections and Objections to Specific Definitions by reference. Plaintiffs object to this interrogatory to the extent it purports to be a single interrogatory as it contains multiple and distinct subparts. Plaintiffs further object to this interrogatory to the extent it purports to be HyperBranch's second interrogatory. HyperBranch previously served Interrogatory Nos. 1-6 on October 23, 2015, and Interrogatory Nos. 7-8 on December 9, 2015. Thus, this interrogatory is HyperBranch's tenth interrogatory. Plaintiffs further object to this interrogatory as being unreasonably cumulative or duplicative, or already known to HyperBranch. *See* Plaintiffs' Responses and Supplemental Responses to Interrogatory Nos. 1 and 8 and Rebuttal Expert Report of Dr. Jimmy Mays, hereby incorporated by reference in their entirety. Plaintiffs further object to this interrogatory to the extent it seeks the disclosure

of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs further object to the interrogatory as overbroad and unduly burdensome and premature at this stage of the litigation in that it requests identification of “all of the factual and legal bases for that contention, and identify all documents and evidence you claim supports that contention.” .” Plaintiffs further object to this interrogatory as premature and irrelevant to the extent it is a contention interrogatory that seeks to impose a burden on Plaintiffs to provide a rebuttal position on the effective filing date of each claim prior to the disclosure of any invalidity contention by the Defendant that puts at issue the effective filing date of any claim on which Defendant has the burden of proof and is required to provide its full and complete invalidity contentions. Validity of the claims is presumed by the issuance of the patent. Defendant bears the burden of establishing through its invalidity contentions that there is an issue as to validity that would require Plaintiffs to prove an earlier effective filing date. To date, Defendants validity contentions have not met that burden. Plaintiffs further object to this Interrogatory to the extent it contains subparts which, together with the other Interrogatories, exceed the limit under the Federal Rules. Plaintiffs also object to this interrogatory to the extent it calls for legal argument and/or expert testimony, which Plaintiffs may provide, in due course and in accordance with the Court’s Scheduling Order.

Subject to and without waiving its objections, Plaintiffs rely on the disclosures provided in the patents-in-suit including the related U.S. applications provided on the front of each of the patents in suit to provide an effective filing date for each of the claims. Particularly, the related U.S. applications listed on the face of the patents-in-suit show that the effective filing date for many of the limitations found in the claims of the patents-in-suit may extend back to at least as

early as December 4, 1998 and possibly as early as September 23, 1996. For example, many of the limitations claimed in the patents-in-suit can expressly be found in the text of the related U.S. applications. (*See, e.g.*, visualization agent, precursors, biodegradable polymers, biodegradable polymeric crosslinkers, nucleophilic functional groups, electrophilic functional groups, hydrogel film thickness, and many others). Plaintiffs further respond that they have produced non-privileged documents pursuant to Federal Rule of Civil Procedure 33(d) for which the burden of deriving or ascertaining the answer will be substantially the same for HyperBranch as it is for plaintiffs, namely the patents-in-suit, the patents and applications from which the patents-in-suit claim priority, and prosecution histories of these patents and patent applications.

Plaintiffs also identify Exhibits 57 and 58 to the previous deposition of the inventors along with the transcripts of those depositions (i.e., Amar Sawhney and Steven Bennett) as providing further information related to the effective filing date of the claims of the patents-in-suit. *See, e.g.*, Steve Bennett deposition transcript at pp. 147-48.

Investigation of the facts is ongoing and Plaintiffs reserve the right to supplement this response to identify additional information and/or documents as more facts arise in discovery and as rebuttal if Defendant meets its burden of setting forth a preliminary contention of invalidity that puts at issue the effective filing date of one or more claims of the patents-in-suit in accordance with the rules and the Scheduling Order in this matter..

INTERROGATORY NO. 3 [11]. On a claim-by-claim basis, describe in detail the complete basis for Your contention that each Asserted Claim is not invalid in view of Defendant's invalidity contentions.

OBJECTION AND ANSWER TO INTERROGATORY NO. 3 [11]:

Plaintiffs incorporate their General Objections and Objections to Specific Definitions by reference. Plaintiffs object to this interrogatory to the extent it purports to be a single interrogatory as it contains multiple and distinct subparts. Plaintiffs further object to this

interrogatory to the extent it purports to be HyperBranch's third interrogatory. HyperBranch previously served Interrogatory Nos. 1-6 on October 23, 2015, and Interrogatory Nos. 7-8 on December 9, 2015. Thus, this interrogatory is HyperBranch's eleventh interrogatory. Plaintiffs further object to this interrogatory as being unreasonably cumulative or duplicative, or already known to HyperBranch. *See* Response to HyperBranch Interrogatory Nos. 4 and 7 and Rebuttal Expert Report of Dr. Jimmy Mays. Plaintiffs further object to this interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs further object to the interrogatory as overbroad and unduly burdensome and premature at this stage of the litigation in that it requests identification of "describe in detail the complete basis for Your contention." Plaintiffs further object to this interrogatory as premature, irrelevant, overbroad, and unduly burdensome to the extent it is a contention interrogatory that seeks to impose a burden on Plaintiffs to provide a rebuttal position on the validity of each claim prior to the disclosure of any invalidity contention by the Defendant that puts at issue the validity of the claim which Defendant has the burden of proof and is required to provide its full and complete invalidity contentions. Validity of the claims is presumed by the issuance of the patent. Defendant bears the burden of establishing through its invalidity contentions that there is an issue as to validity that would require Plaintiffs to prove a rebuttal position. To date, Defendants validity contentions have not met that burden. Plaintiffs also object to this interrogatory as premature, irrelevant, overbroad, and unduly burdensome as Defendant's present invalidity contentions do not provide the complete factual basis for its invalidity contentions for which it bears the burden of proof. Plaintiffs also object to this

interrogatory to the extent it calls for legal argument and/or expert testimony, which Plaintiffs may provide, in due course and in accordance with the Court's Scheduling Order.

Investigation of the facts is ongoing and the Defendants have not provided their contentions sufficient to put at issue the presumption of validity accorded the claims of a duly issued patent. Plaintiffs reserve the right to supplement this response to identify additional information and/or documents as more facts arise in discovery and in rebuttal to any properly asserted contention of invalidity initially raised by Defendants, to which it has the burden of proof, as required by the Rules and the Scheduling Order in this matter.

INTERROGATORY NO. 4 [12]. Describe in detail all rights that have been held in the Asserted Patents, including a description of the histories of such rights, the persons or entities holding such rights, and all agreements and other documents reflecting such rights (identified by Bates numbers).

OBJECTION AND ANSWER TO INTERROGATORY NO. 4 [12]:

Plaintiffs incorporate their General Objections and Objections to Specific Definitions by reference. Plaintiffs object to this interrogatory to the extent it purports to be a single interrogatory as it contains multiple and distinct subparts. Plaintiffs further object to this interrogatory to the extent it purports to be HyperBranch's fourth interrogatory. HyperBranch previously served Interrogatory Nos. 1-6 on October 23, 2015, and Interrogatory Nos. 7-8 on December 9, 2015. Thus, this interrogatory is HyperBranch's twelfth interrogatory. Plaintiffs also object to this interrogatory to the extent it is overly broad and unduly burdensome as being duplicative of previous HyperBranch Interrogatory No. 5. Plaintiffs further object to this interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs further object to the interrogatory as overbroad and unduly burdensome in that it requests that Plaintiffs "[d]escribe in

detail all rights that have been held in the Asserted Patents . . . and all agreements and other documents reflecting such rights.”

Subject to and without waiving its objections, Plaintiffs respond by incorporating by reference in their entirety the previous responses and supplements thereto to HyperBranch Interrogatory No. 5. The original rights in the earliest priority documents set forth on the face of the patents-in-suit resided with Mr. Chandrashekhar P. Pathak and commenced as of the filing dates of each of the respective filing dates of the provisional applications identified on the faces of the patents-in-suit. These rights were transferred by Mr. Pathak on September 18, 1998. The last significant transfer of any rights in the patents in suit occurred in 2013, the same year where some rights in the patents-in-suit were effectively transferred to plaintiffs Integra LifeSciences Corp. and Integra LifeSciences Sales LLC via the Stock Purchase Agreement of Covidien Group S.A.R.L. by Integra Life Sciences Corporation. Plaintiffs further respond that that they have produced non-privileged documents pursuant to Federal Rule of Civil Procedure 33(d) for which the burden of ascertaining the above requested information is substantially the same for HyperBranch as it is for Plaintiffs. These documents include, for example, the documents identified in Plaintiffs Objections and Response to HyperBranch Interrogatory No. 5 (and supplemental responses thereto) along with the following documents: INT00294034-54, INT00650909-18, INT00651004-05, INT00704790-805, INT00637241-91, INT00477543-93, INT00289244-46, INT00481381-504, INT00289335-42, INT00283427-29, INT00289347-68, INT00289426-46, INT00284501-08, INT00289402-25, INT00704658-723, INT00704724-89, INT00635834-INT00636011, INT00294242-61, and INT00635902-61. Investigation of the facts is ongoing and Plaintiffs reserve the right to supplement this response to identify additional information and/or documents as more facts arise in discovery in accordance with the Rules

INTERROGATORY NO. 5 [13]. Describe in detail the amount, method of calculation, and all facts and evidence supporting any calculation for any damages You claim in this Action, and specifically identify and explain the damages suffered by each particular Plaintiff.

OBJECTION AND ANSWER TO INTERROGATORY NO. 5 [13]:

Plaintiffs incorporate their General Objections and Objections to Specific Definitions by reference. Plaintiffs object to this interrogatory to the extent it purports to be a single interrogatory as it contains multiple and distinct subparts. Plaintiffs further object to this interrogatory to the extent it purports to be HyperBranch's fifth interrogatory. HyperBranch previously served Interrogatory Nos. 1-6 on October 23, 2015, and Interrogatory Nos. 7-8 on December 9, 2015. Thus, this interrogatory is HyperBranch's thirteenth interrogatory. Plaintiffs further object to this interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs also object to this interrogatory to the extent it constitutes a contention interrogatory that is overly broad, unduly burdensome, and premature at this stage of discovery. Plaintiff further object to this Interrogatory as seeking information that is properly the subject of expert discovery and expert testimony in advance of the schedule set for the disclosure of expert reports and expert discovery as set forth in the Scheduling Order entered by the Court. Plaintiffs reserve the right to supplement this response to identify additional information and/or documents as more facts arise in discovery in accordance with the Rules.

Subject to and without waiver of the foregoing objections and general objections, Plaintiffs respond that such computations cannot be completed until full and complete information is obtained from Defendant. In this case, damages cannot be computed by providing a monetary number as Plaintiffs damages includes aspects for which monetary damages are insufficient to account for the losses due to Defendant's infringing activity. For infringement in

the United States, the monetary damages that only encompass a small portion of the total harm suffered by plaintiffs and would be equal to at least plaintiff's lost profits (or no less than a reasonable royalty) and damages outside of the United States are not less than a reasonable royalty in accordance with 35 U.S.C. §284. Plaintiffs also believe that discovery will establish that this is a case of willful infringement due at least in part to Defendant's receiving notice of infringement in January 2015 and defendant willfully disregarding that notice coupled with Defendant's continuing and increasing infringement after receiving notice of infringement. At least Defendant's willful infringement makes this an exceptional case which warrants Plaintiffs to recover up to 3 times their actual damages and their attorneys fees along with pre and post judgment interest and costs. Investigation of the facts is ongoing and Plaintiffs reserve the right to supplement this response to identify additional information and/or documents as more facts arise in discovery in accordance with the Rules.

INTERROGATORY NO. 6 [14]. Describe the complete factual and legal basis for Your assertions that any alleged infringement by Defendant is willful.

OBJECTION AND ANSWER TO INTERROGATORY NO. 6 [14]:

Plaintiffs incorporate their General Objections and Objections to Specific Definitions by reference. Plaintiffs object to this interrogatory to the extent it purports to be HyperBranch's sixth interrogatory. HyperBranch previously served Interrogatory Nos. 1-6 on October 23, 2015, and Interrogatory Nos. 7-8 on December 9, 2015. Thus, this interrogatory is HyperBranch's fourteenth interrogatory. Plaintiffs further object to this interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs further object to this Interrogatory as it constitutes a premature contention interrogatory that is overbroad and unduly burdensome and premature at this stage of

the litigation in that it requests identification of “the complete factual and legal basis for Your assertions that any alleged infringement is willful.” Subject to and without waiver of the foregoing specific and general objections, Plaintiffs respond that discovery will establish that this is a case of willful infringement due at least in part to Defendant’s receiving notice of infringement in January 2015 and defendant willfully disregarding that notice coupled with Defendant’s continuing and increasing infringement after receiving notice of infringement. Plaintiffs further incorporate by reference their response to Interrogatory No. 13 as if fully recited herein. Investigation of the facts is ongoing and Plaintiffs reserve the right to supplement this response to identify additional information and/or documents as more facts arise in discovery in accordance with the Rules.

INTERROGATORY NO. 7 [15]. Describe the complete factual and legal basis for Your assertion that this is an exceptional case under 35 U.S.C. § 285.

OBJECTION AND ANSWER TO INTERROGATORY NO. 7 [15]:

Plaintiffs incorporate their General Objections and Objections to Specific Definitions by reference. Plaintiffs object to this interrogatory to the extent it purports to be HyperBranch’s seventh interrogatory. HyperBranch previously served Interrogatory Nos. 1-6 on October 23, 2015, and Interrogatory Nos. 7-8 on December 9, 2015. Thus, this interrogatory is HyperBranch’s fifteenth interrogatory. Plaintiffs further object to this interrogatory to the extent it seeks the disclosure of information protected by the attorney-client privilege, attorney work-product doctrine, common interest privilege, or any other applicable privilege or protection, as provided by any applicable law. Plaintiffs further object to the interrogatory as overbroad and unduly burdensome and premature at this stage of the litigation in that it requests identification of “the complete factual and legal basis for Your assertion.” Plaintiffs respond that this is an exceptional case at least because Defendants infringement has been willful and incorporate their

response to Interrogatory No. 13 as if set forth herein. Investigation of the facts is ongoing and Plaintiffs will supplement this response to identify additional information and/or documents as more facts arise in discovery in accordance with the Rules.

AS TO OBJECTIONS ONLY:

DATED: October 27, 2016

/s/ Karen L. Pascale

An Attorney for Plaintiffs, Integra LifeSciences Corp., Integra LifeSciences Sales LLC, Confluent Surgical, Inc., and Incept LLC

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Telephone (312) 463-5000

CERTIFICATE OF SERVICE

I, Karen L. Pascale, Esquire, hereby certify that on October 27, 2016, I caused true and correct copies of the foregoing document to be served upon the following counsel of record by e-mail:

For Defendant HyperBranch Medical Technology, Inc.:

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------------	--------------------------------

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/s/ Karen L. Pascale

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*Attorneys for Plaintiffs Integra LifeSciences Corp.,
Integra LifeSciences Sales LLC, Confluent Surgical
Inc., and Incept LLC*

Exhibit 5

**UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION**

BENEFICIAL INNOVATIONS, INC.

vs.

AOL, LLC, ET AL.

§
§
§
§
§

CASE NO. 2:07-CV-555-TJW-CE

ORDER

Pending before the court is the plaintiff Beneficial Innovations, Inc.'s ("Beneficial") motion to compel interrogatory responses from the defendants Google Inc. and Youtube, LLC (collectively, "Google") (Dkt. No. 253). The court GRANTS in part and DENIES in part Beneficial's motion to compel. Within ten days of this order, Google must provide Beneficial with full and complete answers to Beneficial's interrogatories seeking Google's non-infringement contentions. Google is not required, however, to disclose its experts' opinions in advance of the deadline for serving expert reports.

SIGNED this 26th day of May, 2010.


CHARLES EVERINGHAM IV
UNITED STATES MAGISTRATE JUDGE

Exhibit 6

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

BENEFICIAL INNOVATIONS, INC.,	§	
	§	
Plaintiff,	§	
	§	
v.	§	Civil Action No: 2:07-CV-555 (TJW/CE)
	§	
AOL LLC, THE DALLAS MORNING	§	
NEWS, INC., GOOGLE INC., IGN	§	
ENTERTAINMENT, INC., MORRIS	§	
COMMUNICATIONS COMPANY, LLC,	§	
TRIBUNE INTERACTIVE, INC., YAHOO!	§	
INC., and YOUTUBE, LLC,	§	
	§	
Defendants.	§	

**OPPOSITION OF DEFENDANTS GOOGLE INC. AND YOUTUBE, LLC
TO PLAINTIFF’S MOTION TO COMPEL INTERROGATORY RESPONSES**

Defendants Google Inc. and YouTube, LLC (collectively referred to as “Google”) present this Opposition to Plaintiff’s Motion to Compel Interrogatory Responses from Google and YouTube (“Plaintiff’s Motion”) and respectfully request that this Court enter an Order denying Plaintiff’s Motion.

INTRODUCTION

Plaintiff’s Motion is both completely unnecessary and a transparent effort to advance the date for receiving expert discovery, in violation of both the Court’s Docket Control Order and this Court’s previous decision in *Jacobs Chuck Mfg. Co. v. Shandong Weida Machinery*, No. 2:05-cv-185 (E.D. Tex. Aug. 18, 2006) (order denying motion to compel) (attached as Exhibit 1 to the Decl. of Mark G. Matuschak in Opp. to Pl.’s Mot. to Compel Interrog. Responses (“Matuschak Decl.”)).

Plaintiff’s Motion relates to two identical interrogatories requesting that Google “[s]et forth in specific detail each fact, opinion, argument, inference, and Document that supports your

contention that you have not infringed any asserted claim” of each of the two patents-in-suit. As Plaintiff well knows, however, such interrogatories are premature because they contravene established discovery time frames under the Patent Rules (and, accordingly, the Docket Control Order in this case), and improperly – and explicitly – seek the early disclosure of expert discovery. (*See Jacobs Chuck*, Matuschak Decl. Ex. 1 at 1-2. & n. 1.) Not surprisingly, while mentioning *Jacobs Chuck* in passing, Plaintiff never attempts to address this Court’s reasoning in that case, or explain why, in Plaintiff’s view, it should be overruled, ignored, or disregarded. Plaintiff’s brief instead is entirely premised on general principles about open and full discovery, and inaccurate statements about the parties’ discussions concerning these interrogatories.

Second, despite the clarity and direct applicability of *Jacobs Chuck* to this exact circumstance, Google has offered Plaintiff a compromise in a good faith effort to avoid needless motions like this one. Specifically, Google offered to provide Plaintiff with responses to the interrogatories that identify the factual bases for Google’s non-infringement positions. (Matuschak Decl. Ex. 2 at 2.) Plaintiff, however, was not satisfied, and demanded instead that Google agree to the entry of a Court Order requiring a “full response” to the interrogatory, including Plaintiff’s request for all “opinions” relating to non-infringement. (*Id.* at 1-2.) This makes plain that, despite its protestations to the contrary, Plaintiff is primarily interested in requiring the early disclosure of Google’s expert opinions regarding non-infringement. Plaintiff is not entitled to that at this stage of the proceedings, as Google’s expert report on non-infringement is not due for another three months, on August 13, 2010.

Plaintiff’s Motion should be denied because it prematurely and improperly seeks expert discovery in contravention of the discovery timetable set forth in the Court’s Docket Control Order, and in direct contravention of this Court’s decision in *Jacobs Chuck*.

BACKGROUND

The Docket Control Order in this matter directs the “[p]arty with the burden of proof to designate Expert Witnesses other than claims construction” and to serve such expert witness’ reports on July 16, 2010. (Docket Control Order (May 18, 2009) at 2 [Dkt. No. 151].) Thereafter, rebuttal expert witness designations and rebuttal expert witness reports are due on August 13, 2010. (*Id.*) Discovery closes on September 24, 2010. (*Id.*)

Plaintiff seeks to compel a response to the following contention interrogatories served on Google:

Set forth in specific detail each fact, opinion, argument, inference, and Document that supports your contention that you have not infringed any asserted claim of the ‘366 Patent (including the name, address, and telephone number of each person who has firsthand knowledge or possession of each such fact, opinion, and Document).

Set forth in specific detail each fact, opinion, argument, inference, and Document that supports your contention that you have not infringed any asserted claim of the ‘702 Patent (including the name, address, and telephone number of each person who has firsthand knowledge or possession of each such fact, opinion, and Document).

(Google’s Objections and Responses to Pl.’s First Set of Interrogs. to Defs. (attached as Exhibit 2 to the Declaration of Julien A. Adams in supp. of Beneficial Innovations’ mot. to compel interrog. responses from Google and YouTube [sic]) (attached to Plaintiff’s Motion (filed April 27, 2010) [Dkt. No. 253]) (“Adams Decl.”) at 4-5.) Google objected to these interrogatories as “premature and in conflict with the Court’s Docket Control Order and Local Patent Rules” and as, among other things, seeking privileged information and “prematurely seek[ing] expert discovery,” citing the Court’s *Jacobs Chuck* decision. (*Id.* at 4-6.) Google stated that it would “provide such responsive information as and when required by the Court’s Docket Control Order and Local Patent Rules.” (*Id.* at 5-6.)

On July 21 and 27, 2009, well before claim construction discovery, Plaintiff initiated two meet-and-confers regarding Google's objections to these interrogatories. (Matuschak Decl. ¶ 5.) At that time, Google referred Plaintiff to the Court's *Jacobs Chuck* decision, and stood on its objections. Plaintiff did not file any motion. (Matuschak Decl. ¶ 6.)

Following this Court's claim construction decision, Plaintiff initiated yet another meet-and-confer on the same issue, although it had presumably read the Court's *Jacobs Chuck* decision. (Matuschak Decl. ¶ 7.) Though multiple parties participated in this meet-and-confer, Plaintiff claims that each of them said exactly the same thing and that Google promised, for some inexplicable reason in light of *Jacobs Chuck*, to provide "a response within a reasonable time" and without regard to the Court's Docket Control Order time frames for expert discovery. (Plaintiff's Motion at 2.) This is simply not true. Google's position always has been that these interrogatories are premature efforts to accelerate expert discovery, and that Google would answer these interrogatories consistently with the Court's Docket Control Order. (Matuschak Decl. ¶ 7.)

Nevertheless, solely in an effort to avoid further unnecessary motion practice, on April 28, 2010, following the filing of Plaintiff's Motion, counsel for Google made the following proposal:

Google will answer the interrogatories in question at least five (5) days before the mutually agreeable scheduled date for the Rule 30(b)(6) deposition of Google that you have recently noticed (please note that we'll likely have to adjust that date and we may have multiple potential witnesses to respond to it, not all of whom may be available on the same day). If this is acceptable to you, please let us know.

(Matuschak Decl. ¶ 8, Ex. 2 at 2.) In response, Plaintiff's counsel insisted that the parties must "submit *a stipulated order* to resolve the pending motion that says *Google will serve a full response* to the rogs [sic] by the date certain." (*Id.* at ¶ 9, Ex. 2 at 1-2 (emphasis added).)

ARGUMENT

Plaintiff's Motion should be denied because it prematurely seeks attorney work product and expert discovery, contrary to the schedule set forth in the Court's Docket Control Order and the Local Patent Rules, and contrary to this Court's explicit decision on this point in *Jacobs Chuck*.

A. Plaintiff's Contention Interrogatories are Premature and Improper

Interrogatories are contention interrogatories to the extent that they require an answer that "involves an opinion or contention that relates to fact or the application of law to fact." Fed.R.Civ.P. 33(c). Plaintiff's interrogatories seek the identification of "each fact, opinion, argument, inference, and Document that supports" Google's non-infringement contentions. (Adams Decl. Ex. 2 at 4-5.) Thus, Plaintiff's interrogatories explicitly seek expert conclusions before expert discovery has even begun. This contradicts the timetable established by this Court's Docket Control Order and the Local Patent Rules.

Specifically, the Court's Docket Control Order provides for Google's expert witness report rebutting Plaintiff's allegation of infringement to be served on August 13, 2010. (Docket Control Order (May 18, 2009) at 2 [Dkt. No. 151].) Until that point, it is only Plaintiff – as the party with the burden of proof for infringement – that carries any obligation with regard to disclosure of infringement positions. *See, e.g.*, L.R. 3-1.

This Court has previously addressed precisely this question in *Jacobs Chuck*. In that case, the defendant moved to compel plaintiffs to respond to a contention interrogatory seeking all the reasons why plaintiffs contended that the elements of the asserted claims were not present in the prior art references identified by defendants in their invalidity contentions. (*Jacobs Chuck*, Matuschak Decl. Ex. 1 at 1.) The Court concluded that "if the court required the plaintiffs to

answer such an interrogatory at this stage of the case, the court would run the risk of requiring the disclosure of information protected by the attorney client privilege and work product doctrine.” (*Id.* at 1-2.) The Court made clear that this ruling would apply equally to a plaintiff seeking early contention discovery of a defendant’s non-infringement contentions. (*See id.* at 2 n.1 (“The court sees no reason why this holding would not apply equally to the reverse situation— an interrogatory served by a plaintiff early on in the case asking a defendant to identify all the limitations of an asserted claim that the defendant contends are not found in an accused product.”).)

This case is exactly the situation discussed by this Court in footnote 1 of *Jacobs Chuck*. Plaintiff’s interrogatories explicitly ask for an identification of every opinion supporting Google’s position that it has not infringed the claims of Plaintiff’s asserted patents. (*See Adams Decl. Ex. 2* at 4-5.) As the Court explained in *Jacobs Chuck*, such interrogatories are premature because they contravene established discovery time frames under the Patent Rules and improperly seek the disclosure of privileged and protected attorney evaluations and opinions regarding infringement. (Matuschak Decl. Ex. 1 at 1-2.) Accordingly, Plaintiff’s Motion should be denied as improper and premature, as it seeks to impose obligations on the Google that are contrary to the discovery requirements and timetables of the Court’s Docket Control Order and the Local Patent Rules.

B. Google’s Proposal to Respond to Plaintiff’s Interrogatories Renders Plaintiff’s Motion Unnecessary

Plaintiff’s Motion is also utterly unnecessary, as Google has agreed to respond to the portion of Plaintiff’s interrogatories that seek the factual bases for its non-infringement positions. (*See Matuschak Decl. ¶ 8, Ex. 2* at 2.) As this is the only responsive discovery to which Plaintiff

can legitimately claim entitlement at this time, Plaintiff's Motion should be denied because it is unwarranted for this additional reason.

Specifically, Google has proposed to answer the interrogatories in question on a to-be-agreed-upon date certain, at least five days prior to the upcoming Rule 30(b)(6) deposition of Google. (*Id.*) While Plaintiff has refused to accept this proposal (*see id.* at ¶ 9, Ex. 2 at 1-2), that does not change the fact that Google has already agreed to provide Plaintiff with an identification of the factual bases that Plaintiff seeks. For the reasons discussed in the preceding section, however, Google has never agreed to and should not be required to provide premature expert discovery and work product in the form of opinions, theories, or other evaluation-type information.

CONCLUSION

For the foregoing reasons, Google respectfully requests that the Court enter an Order denying Plaintiff's Motion.

Dated: May 14, 2010

Respectfully submitted,

/s/ Violetta G. Watson
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**ATTORNEYS FOR DEFENDANTS
GOOGLE INC. AND YOUTUBE, LLC**

CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing document was filed electronically in compliance with Local Rule CV-5(a). As such, this notice was served on all counsel who have consented to electronic service on May 14, 2010. Local Rule CV-5(a)(3)(A).

/s/ Violetta G. Watson

Violetta G. Watson

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

BENEFICIAL INNOVATIONS, INC.,	§	
	§	
Plaintiff,	§	
	§	
v.	§	Civil Action No: 2:07-CV-555 (TJW/CE)
	§	
AOL LLC, THE DALLAS MORNING	§	
NEWS, INC., GOOGLE INC., IGN	§	
ENTERTAINMENT, INC., MORRIS	§	
COMMUNICATIONS COMPANY, LLC,	§	
TRIBUNE INTERACTIVE, INC., YAHOO!	§	
INC., and YOUTUBE, LLC,	§	
	§	
Defendants.	§	

DECLARATION OF MARK G. MATUSCHAK
IN OPPOSITION TO PLAINTIFF'S MOTION
TO COMPEL INTERROGATORY RESPONSES

I, Mark G. Matuschak, pursuant to 28 U.S.C. § 1746, declare::

1. I am a partner of the law firm Wilmer Cutler Pickering Hale and Dorr LLP, and lead counsel for Defendants Google Inc. and YouTube, LLC in the above-captioned matter. I am a member in good standing of the bars of the Commonwealth of Massachusetts, the U.S. District Court for the District of Massachusetts, the U.S. District Court for the District of Colorado, and the U.S. Court of Appeals for the First, Second, Third and Federal Circuits.
2. I submit this declaration in opposition to Plaintiff Beneficial Innovations, Inc.'s Motion to Compel Interrogatory Responses from Google and YouTube ("Plaintiff's Motion").

3. On June 3, 2009, Plaintiff Beneficial Innovations, Inc. (“Plaintiff”) served its First Set of Interrogatories to Defendants, requesting in Interrogatory Nos. 1 and 2 that Google “[s]et forth in specific detail each fact, opinion, argument, inference, and Document that supports your contention that you have not infringed any asserted claim” of each of the two patents-in-suit. (See Google’s Objections and Responses to Pl.’s First Set of Interrogs. to Defs. (attached as Exhibit 2 to the Decl. of Julien A. Adams in supp. of Beneficial Innovations’ mot. to compel interrog. responses from Google and YouTube sic)) (attached to Plaintiff’s Motion (filed April 27, 2010) [Dkt. No. 253]) (“Adams Decl.”) at 4-5.)
4. On July 14, 2009, Google served its Objections and Responses to Plaintiff’s First Set of Interrogatories. In response to Interrogatory Nos. 1 and 2, Google objected on grounds including:
 - “that it is premature and in conflict with the Court’s Docket Control Order and Local Patent Rules. See *Chuck [sic] Mfg. Co. v. Shandong Weida Machinery, et al.*, No. 2:05-cv-185, Dkt. No. 93 (E.D. Tex. Aug. 18, 2006) (Ward, D.J.) (order denying motion to compel)”
 - “that it seeks the production, identification, or disclosure of information protected by the attorney-client privilege, the work product doctrine, or any other applicable privilege or protection from disclosure”
 - “that it prematurely seeks expert discovery”(Adams Decl. Ex. 2 at 4-5.) Google further stated: “Accordingly, Google will not respond to this interrogatory, but instead will provide such responsive information as and when required by the Court’s Docket Control Order and Local Patent Rules.” (*Id.*)

5. Plaintiff thereafter initiated a meet-and-confer that took place on July 21, 2009, and a follow-up meet-and-confer that took place on July 27, 2009, to discuss Google's objections to these interrogatories.
6. Google maintained its objections during and after the July 21 and July 27, 2009 meet-and-confers, and Plaintiff did not file any motion in response.
7. Following this Court's claim construction decision, Plaintiff initiated another meet-and-confer on the same issue on March 11, 2010. During this meet-and-confer, Google maintained its position that Plaintiff's interrogatories are premature efforts to accelerate expert discovery, and that Google would answer these interrogatories consistently with the Court's Docket Control Order. Google did not promise to provide "a response within a reasonable time," as Plaintiff asserts. (*See* Plaintiff's Motion at 2.)
8. On April 27, 2010, Plaintiff filed its pending Motion to Compel. Since then, in a good faith effort to avoid further unnecessary motion practice, Google offered to provide Plaintiff with responses to the interrogatories that identify the factual bases for Google's non-infringement positions. Specifically, on April 28, 2010, I sent Plaintiff's counsel, Julien A. Adams, an e-mail with the following proposal:

Google will answer the interrogatories in question at least five (5) days before the mutually agreeable scheduled date for the Rule 30(b)(6) deposition of Google that you have recently noticed (please note that we'll likely have to adjust that date and we may have multiple potential witnesses to respond to it, not all of whom may be available on the same day). If this is acceptable to you, please let us know.

Attached hereto as Exhibit 2 is a true and correct copy of my e-mail correspondence with Julien A. Adams, dated August 28, 2010.

9. In response, Mr. Adams refused the proposal, unless Google would agree to “submit *a stipulated order* to resolve the pending motion that says *Google will serve a full response* to the rogs [sic] by the date certain,” including Plaintiff’s request for all opinions, arguments, and inferences. (Ex. 2 at 1-2 (emphasis added).)

I declare under penalty of perjury that the foregoing is true and correct.

Executed on May 14, 2010 in New York, New York.

/s/ Mark G. Matuschak
Mark G. Matuschak

EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

JACOBS CHUCK MANUFACTURING CO. §

Vs. § CIVIL ACTION NO. 2:05-CV-185

SHANDONG WEIDA MACHINERY, ET AL. §

ORDER

One World moves to compel the plaintiffs to respond to Interrogatory No. 13. Interrogatory 13 asks the plaintiffs to:

[i]dentify each element of the asserted claims of the ‘254 and ‘345 patents that Plaintiffs contend is not disclosed in each of the prior art references cited in Defendants’ Disclosure of Preliminary Invalidity Contentions and Attachment A thereof, and include the basis and all reasons why Plaintiffs contend such element(s) are not present.

One World contends that this interrogatory is permissible and serves to narrow the claim construction process. Plaintiffs contend that the interrogatory requires the disclosure of attorney client and work product protected information and, in any event, is premature under the docket control order.

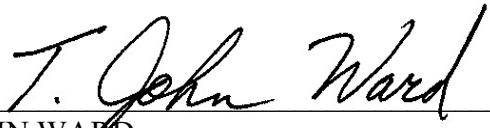
The court agrees with the plaintiffs that the interrogatory is premature and, for that reason, will deny the motion to compel. A requirement that a party provide contentions of this sort early in the litigation is in tension with the established time frames for declaring claim construction positions provided by the Patent Rules. Moreover, if the court required the plaintiffs to answer such an interrogatory at this stage of the case, the court would run the risk of requiring the disclosure of

information protected by the attorney client privilege and the work product doctrine. A complete answer to this interrogatory would require the disclosure of the attorney's evaluation of the cited prior art, in light of several possible claim constructions. For these reasons, the court will deny the motion to compel at this time.

This order is without prejudice to One World's right to renew its motion after the court issues the claim construction opinion. As the parties acknowledge, the docket control order provides a deadline for the plaintiffs to serve expert reports in opposition to the invalidity opinions advanced by the defendants' experts. Thus, the plaintiffs eventually will have to declare their positions on invalidity—at least if they hope to offer expert testimony at trial. Presumably included among these positions will be a discussion of various limitations contended to be novel over the asserted art. The court defers expert reports until after the issuance of the claim construction opinion in part because the court believes that it benefits the experts to know the scope of the claims before they render their opinions. Deferral of the obligation to answer this type of contention interrogatory is also appropriate. As such, One World is not precluded from moving to compel a further answer to this interrogatory after the court issues its claim construction ruling.¹ The court expresses no opinion on the level of detail required to respond properly to that portion of the interrogatory asking the plaintiffs to “include the basis and all reasons” why they contend certain limitations are not found in the prior art.

¹ The court sees no reason why this holding would not apply equally to the reverse situation—an interrogatory served by a plaintiff early on in the case asking a defendant to identify all of the limitations of an asserted claim that the defendant contends are not found in an accused product.

SIGNED this 18th day of August, 2006.



T. JOHN WARD
UNITED STATES DISTRICT JUDGE

EXHIBIT 2

From: Julien Adams [mailto:julien@dovellaw.com]
Sent: Wednesday, April 28, 2010 11:48 PM
To: Matuschak, Mark
Cc: Hutchins, Kate
Subject: RE: Adams to Matuschak 4'28'2010 re Activity in Case 2:07-cv-00555-TJW-CE Beneficial Innovations, Inc. v. AOL, LLC. et al Motion to Compel

Mark,

That is unfortunate. I guess we are back to where we started.

Sincerely,

Julien Adams
201 Santa Monica Boulevard
Suite 600
Santa Monica, CA 90104
(310) 656-7066
(310) 656-7069

From: Matuschak, Mark [mailto:Mark.Matuschak@wilmerhale.com]
Sent: Wednesday, April 28, 2010 6:48 PM
To: Julien Adams
Cc: Hutchins, Kate
Subject: RE: Adams to Matuschak 4'28'2010 re Activity in Case 2:07-cv-00555-TJW-CE Beneficial Innovations, Inc. v. AOL, LLC. et al Motion to Compel

Julien -

We'd propose that we do 1 and 2. We're not agreeing to a stipulated order. You can either withdraw the motion without prejudice or we can agree to file something that says the parties are working out the issue and extend the time for our response until some time after the answer is served.

Thanks,
Mark

From: Julien Adams [mailto:julien@dovellaw.com]
Sent: Wednesday, April 28, 2010 9:28 PM
To: Matuschak, Mark
Cc: Hutchins, Kate
Subject: Adams to Matuschak 4'28'2010 re Activity in Case 2:07-cv-00555-TJW-CE Beneficial Innovations, Inc. v. AOL, LLC. et al Motion to Compel

Mark,

I'm not sure why you consider the motion unnecessary. Anyway, I would propose the following:

1. We set the date for the beginning of the 30(b)(6) deposition(s) - to the extent that we may have to conduct them on multiple days.

2. Once we have the first date set, then we will have a date certain for your response.
3. Once we have the date certain for the response, we submit a stipulated order to resolve the pending motion that says Google will serve a full response to the rogs by the date certain.

If you agree with this procedure, please let me know as soon as possible the date or dates you have in mind for the depositions.

Sincerely,

Julien A. Adams
201 Santa Monica Boulevard
Suite 600
Santa Monica, Ca 90401
(310) 656-7066 phone
(310) 656-7069 fax

From: Matuschak, Mark [mailto:Mark.Matuschak@wilmerhale.com]
Sent: Wednesday, April 28, 2010 5:17 PM
To: Julien Adams
Cc: Hutchins, Kate
Subject: FW: Activity in Case 2:07-cv-00555-TJW-CE Beneficial Innovations, Inc. v. AOL, LLC. et al Motion to Compel

Julien -

In order to avoid what we believe is a completely unnecessary motion (see below), Google proposes the following: Google will answer the interrogatories in question at least five (5) days before the mutually agreeable scheduled date for the Rule 30(b)(6) deposition of Google that you have recently noticed (please note that we'll likely have to adjust that date and we may have multiple potential witnesses to respond to it, not all of whom may be available on the same day). If this is acceptable to you, please let us know.

Regards,
Mark

From: txedCM@txed.uscourts.gov [mailto:txedCM@txed.uscourts.gov]
Sent: Tuesday, April 27, 2010 6:34 PM
To: txedcmcc@txed.uscourts.gov
Subject: Activity in Case 2:07-cv-00555-TJW-CE Beneficial Innovations, Inc. v. AOL, LLC. et al Motion to Compel

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U.S. District Court [LIVE]

Eastern District of TEXAS

Notice of Electronic Filing

The following transaction was entered by Adams, Julien on 4/27/2010 at 5:33 PM CDT and filed on 4/27/2010

Case Name: Beneficial Innovations, Inc. v. AOL, LLC. et al

Case Number: [2:07-cv-00555-TJW-CE](#)

Filer: Beneficial Innovations, Inc.

Document Number: [253](#)

Docket Text:

Opposed MOTION to Compel *Interrogatory responses from Google and Youtube* by Beneficial Innovations, Inc.. (Attachments: # (1) Affidavit of Julien Adams, # (2) Exhibit 1, # (3) Exhibit 2, # (4) Exhibit 3, # (5) Exhibit 4, # (6) Text of Proposed Order)(Adams, Julien)

2:07-cv-00555-TJW-CE Notice has been electronically mailed to:

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The following document(s) are associated with this transaction:

Document description:Main Document

Original filename:n/a

Electronic document Stamp:

[STAMP dcecfStamp_ID=1041545818 [Date=4/27/2010] [FileNumber=6394463-0]
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Document description:Affidavit of Julien Adams

Original filename:n/a

Electronic document Stamp:

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Document description:Exhibit 1

Original filename:n/a

Electronic document Stamp:

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Document description:Exhibit 2

Original filename:n/a

Electronic document Stamp:

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Document description:Exhibit 3

Original filename:n/a

Electronic document Stamp:

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Document description:Exhibit 4

Original filename:n/a

Electronic document Stamp:

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Document description:Text of Proposed Order

Original filename:n/a

Electronic document Stamp:

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IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

BENEFICIAL INNOVATIONS, INC.,

Plaintiff,

V.

AOL LLC, THE DALLAS MORNING NEWS, INC., GOOGLE INC., IGN ENTERTAINMENT, INC., MORRIS COMMUNICATIONS COMPANY, LLC, TRIBUNE INTERACTIVE, INC., YAHOO! INC., and YOUTUBE, LLC,

Defendants.

Civil Action No: 2:07-cv-555 (TJW/CE)

ORDER DENYING MOTION TO COMPEL

Having considered Plaintiff Beneficial Innovations, Inc.’s Motion to Compel Interrogatory Responses from Google and YouTube and the parties’ arguments regarding that Motion, the Court hereby **DENIES** said Motion.

Exhibit 7

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

INTEGRA LIFESCIENCES CORP.,)	
INTEGRA LIFESCIENCES SALES LLC,)	
CONFLUENT SURGICAL, INC., and)	
INCEPT LLC,)	
)	C.A. No. 15-819 (LPS) (CJB)
Plaintiffs,)	
)	
v.)	
)	
HYPERBRANCH MEDICAL)	
TECHNOLOGY, INC.,)	
)	
Defendant.)	

HYPERBRANCH MEDICAL TECHNOLOGY, INC.’S INITIAL INVALIDITY CONTENTIONS

In accordance with paragraph 7(d) of the Scheduling Order entered in this action (D.I. 173) and paragraph 4(c) of this district’s Default Standard for Discovery, Including Discovery of Electronically Stored Information (“ESI”), Defendant HyperBranch Medical Technology, Inc. (“HyperBranch”) hereby provides the following initial invalidity contentions to Plaintiffs Integra LifeSciences Corp., Integra LifeSciences Sales LLC, Confluent Surgical, Inc. and Incept LLC (collectively, “Plaintiffs”).

In their “Preliminary Infringement Contentions” served on September 30, 2016, Plaintiffs asserted that HyperBranch infringes the following 105 claims of the Patents-in-Suit:

Patent	Asserted Claims
7,009,034	1, 3-6, and 9-21
7,592,418	1, 3-11, 13-16, and 22-30
7,332,566	1, 3, 4, 6-12, 14-16, 18-25, 27, 28, and 30-38
6,566,406	1, 2, 6-8, 10, 12, 14-16, 19, 21, and 23-25
8,003,705	1, 4-6, 11-13, 16, and 19
8,535,705	1, 5-7, 9, 12, 15, and 17

HyperBranch alleges that the claims of U.S. Patent Nos. 7,009,034 (the “’034 patent”), 7,592,418 (the “’418 patent”), 7,332,566 (the “’566 patent”), 6,566,406 (the “’406 patent”),

8,003,705 (the “3,705 patent”), and 8,535,705 (the “5,705 patent”) (collectively, “the Patents-in-Suit”) asserted by Plaintiffs (the “Asserted Claims”) are invalid at least for the reasons set forth herein. HyperBranch’s investigation is ongoing. Claim construction has not been completed, fact and expert depositions remain to be taken, and Plaintiffs’ production of documents and materials, as well as Plaintiffs’ responses to interrogatories and requests for admission, is incomplete and deficient. Further review of discovery produced by Plaintiffs, review of documents produced by any third party, deposition testimony, the investigation and analysis of any testifying expert, or the results of any future investigation may require HyperBranch to further supplement these contentions. HyperBranch reserves the right to further supplement, revise, or modify its contentions without prejudice. HyperBranch hereby incorporates any existing or future expert reports, declarations, or briefing on claim construction, invalidity, and/or infringement filed by HyperBranch that relate to the invalidity of Plaintiffs’ asserted claims, including without limitation all documents related to the preliminary injunction and any proceedings before the United States Patent and Trademark Office.

I. The Asserted Claims Are Invalid Under 35 U.S.C. § 112¹

All of the Asserted Claims are invalid under 35 U.S.C. § 112 for lack of written description, lack of enablement, and/or indefiniteness.

¹ All section references are to the U.S. Patent Act, 35 USCS § 1 et seq. This title was amended by the Leahy-Smith America Invents Act (“AIA”) of September 16, 2011. *See* Pub. L. 112-29 (2011). Under the terms of that act, the Patents-in-Suit are governed by the pre-AIA formulation of Title 35. Accordingly, reference is made to sections of the act as they were enumerated prior to the AIA amendments.

A. Legal Standards

1. Written Description

“The specification shall contain a written description of the invention and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same” 35 U.S.C. § 112, ¶ 1. “Written description is a question of fact, judged from the perspective of one of ordinary skill in the art as of the relevant filing date.” *Falkner v. Inglis*, 448 F.3d 1357, 1363 (Fed. Cir. 2006). To satisfy the written description requirement of 35 U.S.C. § 112, “the disclosure of the application relied upon [must] reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.” *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). “Possession” requires that “[t]he four corners of the specification . . . describe an invention understandable to [a] skilled artisan and show that the inventor actually invented the invention claimed.” *Id.* at 1351. The level of detail required to satisfy the written description requirement depends on the scope of the claims and predictability of the relevant technology. *Id.*; see also *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1344 (Fed. Cir. 2011). In an unpredictable art, a higher level of detail is required to show that the inventors possessed what was claimed. See, e.g., *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1229 (Fed. Cir. 1994).

“The written description requirement exists to ensure that inventors do not attempt to preempt the future before it has arrived.” *Billups-Rothenberg*, 642 F.3d at 1036 (Fed. Cir. 2011); *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1306 (Fed. Cir. 2008) (“[t]he written description requirement operates as a timing mechanism to ensure fair play in the presentation of

claims after the original filing date and to guard against manipulation of that process by the patent applicant”); *Abbvie Deutschland GMBH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1299 (Fed. Cir. 2014) (“requiring a written description of the invention plays a vital role in curtailing claims that have not been invented, and thus cannot be described.”)

For the purposes of written description the invention is “whatever is now claimed.” *See, e.g., PowerOasis*, 522 F.3d at 1311; *Synthes USA, LLC v. Spiral Kinetics, Inc.*, 734 F.3d 1332, 1341 (Fed. Cir. 2013) (“[w]hile broadening claims during prosecution to capture a competitor’s products is not improper, the written description must support the broadened claims”); *see also Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 909 n.2 (Fed. Cir. 2004); *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479 (Fed. Cir. 1998) (claims amended during prosecution that are directed to a distinct invention from that disclosed in the specification were not adequately described).

Determining whether the patent satisfies the written description requirement “requires an objective inquiry into the four corners of the specification.” *Centocor Ortho Biotech, Inc. v. Abbott Laboratories*, 636 F.3d 1341, 1348 (Fed. Cir. 2011) (internal quotations omitted). Each claim limitation must be described in the specification. *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997); *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1347 (Fed. Cir. 2011). A patent “can be held invalid for failure to meet the written description requirement based solely on the face of the patent specification.” *Centocor*, 636 F.3d at 1347.

The written description “must do more than merely disclose that which would render the claimed invention obvious.” *ICU Med., Inc. v. Alaris Med. Sys., Inc.*, 558 F.3d 1368, 1377 (Fed. Cir. 2009); *Univ. of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 926 (Fed. Cir. 2004);

Waldemar Link v. Osteonics, Corp., 32 F.3d 556, 558 (Fed. Cir. 1994) (“one skilled in the art, reading the original specification [must] immediately discern the limitation at issue.”).

“A mere wish or plan for obtaining the claimed invention is not adequate written description.” *Centocor*, 636 F.3d at 1348 (internal quotation omitted); *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1122 (Fed. Cir. 2008); *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) (“The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention”); *see also Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997) (“Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”); *Centocor*, 636 F.3d at 1350-53 (claim to provisional application filing date rejected for lack of disclosure of the claimed subject matter); *Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336, 1349-51 (Fed. Cir. 2013) (claims to species added late in prosecution not supported by specification); *see also Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004) (same).

“[T]he lack of any disclosure of examples may be considered when determining whether the claimed invention is adequately described.” *Boston Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1364 (Fed. Cir. 2011), *affirming Boston Scientific Corp. v. Johnson & Johnson Inc.*, 679 F. Supp. 2d 539, 555 (D. Del. 2010) (“[l]ogically, the inventors could not have described a knowledge that they did not possess.”). A patentee may not rely on information “well-known in the art” to supply the lacking written description in an unpredictable art. *See, e.g., Univ. of Rochester*, 358 F.3d at 927. Information post-dating the filing of the patent is immaterial to written description because one of skill in the art must recognize that the inventors

possessed what they claimed as of the date of filing. *See, e.g. Ariad Pharm, Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1355 (Fed. Cir. 2010).

The *full scope* of claims must be described and enabled. *See PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1311 (Fed. Cir. 2008); *LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1345-46 (Fed. Cir. 2005) (written description requires that the specification demonstrates the inventor possessed the “full scope of the invention”); *Wyeth and Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013) (the *full scope* of the claims must be enabled).

2. Enablement

A patent is invalid if it is not enabled. 35 U.S.C. § 112. The enablement doctrine “prevents both inadequate disclosure of an invention and overbroad claiming that might otherwise attempt to cover more than was actually invented.” *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1380-81 (Fed. Cir. 2012).

Whether the disclosure of a patent specification satisfies the enablement requirement of 35 U.S.C. § 112 is a question of law based on underlying facts. *Auto. Techs. Int’l, Inc. v. BMW of N. Am., Inc.*, 501 F.3d 1274, 1281 (Fed. Cir. 2007); *Nat’l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190 (Fed. Cir. 1999). Enablement is determined as of the effective filing date of the patent’s application. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371-72 (Fed. Cir. 1999).

To satisfy the enablement requirement, the specification must teach one of ordinary skill in the art how to make and use the invention without “undue experimentation.” *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). Factors considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the

presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F.2d at 737.

“[W]hen there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all of the disclosure related to the process is within the skill of the art This specification provides only a starting point, a direction for further research.” *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997); *see also Alza*, 603 F.3d at 941 (no enablement where disclosure requires person of ordinary skill to engage in an iterative, trial-and-error process to practice the claimed invention); *Promega Corp. v. Life Techs. Corp.*, 773 F.3d 1338, 1349, (Fed. Cir. 2014) (no enablement of a broad claim that covers potentially thousands of unrecited STR loci combinations) “[N]ovel aspects of the invention” must be enabled in the patent, not the prior art. *Auto. Techs.*, 501 F.3d at 1283; *see also Alza Corp. v. Andrx Pharmaceuticals, LLC*, 60 F.3d 935, 941 (Fed. Cir. 2010).

Information post-dating the filing of a patent is not relevant to whether the patent complies with the enablement requirement, because one of skill in the art must be able to practice the invention without undue experimentation as of the time the invention was made. *See, e.g., Wyeth*, 720 F.3d at 1384. A patentee cannot rely on the knowledge of one skilled in the art to supply the missing aspects of its invention to satisfy the enablement requirement. *See Auto Techs.*, 501 F.3d at 1283; *see also Genentech, Inc. v. Novo Nordisk*, 108 F.3d 1361, 1366 (Fed. Cir. 1997).

That a claim may cover a finite number of inoperative embodiments and still be valid does not permit the patentee to rely on unclaimed elements to rescue the claim from inoperability. *See, e.g. Nat'l Recovery Tech., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1196-97 (Fed. Cir. 1999); *see also Crown*, 289 F.3d at 1384 n.8 (“the question is whether the scope of enablement conveyed by the disclosure to a [POSA] is commensurate with the scope of protection taught by the claims.”)

The full scope of the claims must be enabled. *See Auto Techs. Int'l, Inc. v. BMW N. Am., Inc.*, 501 F.3d 1274, 1285 (Fed. Cir. 2007) (“We also reject ATI’s argument that because the specification enables one mode of practicing the invention . . . the enablement requirement is satisfied . . . the specification must enable the full scope of the claims”); *see also MagSil*, 687 F.3d at 1384.

3. Indefiniteness

“[A] patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention.” *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2124 (2014); *see also* 35 U.S.C. § 112, ¶ 2 (The Patent Act requires that a patent specification “conclude with one or more claims *particularly pointing out and distinctly claiming* the subject matter which the applicant regards as [the] invention.”) (emphasis added). Under this requirement, “a patent must be precise enough to afford clear notice of what is claimed, thereby apprising the public of what is still open to them.” *Id.* at 2129 (quotations omitted). Invalidating patent claims for indefiniteness is warranted where the claims create “[a] zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims.” *Id.*

(quoting *United Carbon Co. v. Binney & Smith Co.*, 317 U.S. 228, 236, 63 S. Ct. 165, 87 L.Ed. 232 (1942)).

Indefiniteness is a question of law. See *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, Nos. 2012-1567, 2012-1568, 2012-1569, 2012-1570, 2015 WL 3772402, at *3 (Fed. Cir. June 18, 2015). “The internal coherence and context assessment of the patent, and whether it conveys claim meaning with reasonable certainty, are questions of law.” *Id.* The meaning one of skill in the art would attribute term in dispute “in light of its use in the claims, the disclosure in the specification, and the discussion of this term in the prosecution history is a question of law.” *Id.*

The intrinsic record is paramount to an assessment of indefiniteness. *Id.*, at *5 (“Determining the meaning or significance to ascribe to the legal writings which constitute the intrinsic record is legal analysis.”). “Determining the significance of disclosures in the specification or prosecution history is also part of the legal analysis.” *Id.*

A party “cannot transform into a factual matter the internal coherence and context assessment of the patent simply by having an expert offer an opinion on it.” *Id.* Rather, “[t]he meaning one of skill in the art would attribute to [a disputed term] in light of its use in the claims, the disclosure in the specification, and the discussion of this term in the prosecution history is a question of law.” *Id.*

B. The Asserted Claims are Invalid Under 35 U.S.C. § 112

When properly construed, and/or when construed in a manner required by Plaintiffs’ infringement contentions, the following claim elements, in whole, in part, or as they are used in the context of the claims, render the Asserted Claims invalid under § 112: “precursor species”; “visualization agent”; “such that the nucleophilic functional groups and electrophilic functional groups crosslink after contact with the tissue to form a hydrogel”; “at least one substrate coating

surface”; “visualization agent . . . reflecting or emitting light at a wavelength detectable to a human eye”; “means for visualization of the coating by a human eye”; “synthetic materials”; “the hydrogel is hydrolytically biodegradable”; “hydrophilic polymers”; “the hydrogel forms within 60 seconds after contact with the substrate”; “biodegradable hydrogel”; “adherent to the tissue”; “adapted for use”; “tissue of a patient”; “applying the hydrogel onto the tissue until an average thickness is reached in which the color of the hydrogel indicates that a predetermined thickness of hydrogel has been deposited on the tissue”; “predetermined thickness”; “choosing the predetermined thickness”; “about 0.5 to about 4.0 mm”; “precursor”; “reactive precursor species”; “a hydrolytically biodegradable portion such that the hydrogel is biodegradable”; “a polymer composition that crosslinks to form a hydrogel”; “tissue”; “patient”; “selecting a concentration of visualization agent for the polymer composition such that the visualization agent causes a visually observable change that indicates that a crosslinked hydrogel having a predetermined thickness has been formed on the tissue of a patient”; “the polymer composition comprises electrophilic/nucleophilic functional groups”; “electrophilic functional groups”; “nucleophilic functional groups”; “crosslink to each other”; “observable change”; “not being able to see a substrate through the polymer composition”; “not being able to see patterns in a substrate surface through the polymer composition”; “the polymer composition crosslinks to form a hydrogel within about 60 seconds after being applied to a substrate”; “mixing the visualization agent at a selected concentration with reactive precursor species”; “essentially completely degradable”; “selecting a concentration of visualization agent for the polymer composition so that when the hydrogel is applied onto a substrate to reach an average predetermined thickness of the hydrogel, an observable change occurs indicating the predetermined thickness of hydrogel has been deposited on the substrate”; “prone to aqueous

hydrolysis”; “degradable in vitro by exposure to aqueous solution”; “synthetic polymer”; “the hydrogel is free of amino acid sequences of more than about four residues in number”; “after being applied to the substrate”; “the observable change is not being able to see the substrate tissue through the polymer composition, not being able to see patterns in the substrate surface through the polymer composition, the features of the substrate are obscured, or not being able to see the microvasculature on the substrate tissue”; “wherein the observable change is not being able to see through the polymer composition”; “the observable change is not being able to see patterns in the substrate surface through the polymer composition”; “the observable change is that the features of the substrate are obscured”; “the observable change is not being able to see the microvasculature on the substrate tissue”; “the synthetic polymer comprises the plurality of primary amines”; “adherent to the substrate”; “biocompatible visualization agent”; “essentially completely degradable in vivo by hydrolytic degradation”; “the hydrogel having an interior and an exterior”; “the visualization agent being at least partially disposed within the interior”; “the hydrogel comprises chemical groups that are prone to aqueous hydrolysis”; “the visualization agent has a predetermined concentration that indicates a predetermined thickness of the hydrogel as deposited on the substrate”; “after contact with the substrate”; “the predetermined thickness of the hydrogel is indicated by an observable change of not being able to see the substrate tissue through the polymer composition, not being able to see patterns in the substrate tissue surface through the polymer composition, the features of the substrate are obscured, or not being able to see the microvasculature on the substrate tissue”; “reactive precursor species”; “unbleached visualization agent”; “crosslink the reactive precursor species after the mixing”; “having an interior and exterior”; “thereby degradable in vitro by exposure to aqueous solution”; “selecting a concentration of visualization agent for the polymer composition that results in a visually

observable change when the polymer composition is applied to a substrate tissue at a predetermined thickness to form the crosslinked biodegradable hydrogel on the substrate tissue”; “wherein the observable change is not being able to see the substrate tissue through the polymer composition, not being able to see patterns in the substrate tissue surface through the polymer composition, the features of the substrate are obscured, or not being able to see the microvasculature on the substrate tissue”; “adherent to the substrate tissue”; “a reaction product of a synthetic polymer that comprises”; “a synthetic polymer that comprises a plurality of primary amines or primary thiols”; “wherein the reaction product is formed through the crosslinking between the electrophilic the functional groups of the synthetic polymer and the plurality of primary amines or primary thiols in the other synthetic polymer”; “a biocompatible small molecule crosslinker”; “molecular weight”; “providing a synthetic biocompatible functional polymer with a molecular weight of at least about 7 times more than the crosslinker”; “the functional polymer”; “the crosslinker”; “combining the crosslinker and functional polymer to react the crosslinker functional groups with the functional polymer functional groups to form a hydrogel”; “providing a biocompatible small molecule crosslinker”; “a synthetic biocompatible functional polymer having a biodegradable link”; “a molecular weight of 2000 or less”; “a synthetic biocompatible functional polymer having at least two second functional groups and having a molecular weight at least about 7 times more than the small molecule crosslinker”; “the combination of the first and second functional groups results in the formation of the biocompatible crosslinked polymer hydrogel”; “the small molecule crosslinker has at least 3 functional groups”; “at least one biocompatible crosslinker region consisting”; essentially of a crosslinked synthetic crosslinker molecule with a pre-crosslinked molecular weight of less than 2000”; “at least one biocompatible functional polymer region consisting essentially of a

crosslinked synthetic polymer molecule with a pre-crosslinked molecular weight of more than about 7 times the molecular weight of the pre-crosslinked crosslinker molecule”; “the biocompatible crosslinked polymer comprises at least three links between the crosslinker region and the functional polymer region”; “the links are a reaction product of at least one electrophilic functional group with of at least one nucleophilic functional group that react to form the hydrogel”; “the biocompatible crosslinked polymer further comprises at least one biodegradable link”; “joined to the crosslinker by covalent bonds to form a hydrogel”; “a molecular weight of 100 to 2000 when not bonded to the polymer”; “the synthetic polymer being water soluble”; “being of a molecular weight of at least about 7 times the molecular weight of the crosslinker when not bonded with the crosslinker”; “the electrophiles and nucleophiles cause the biocompatible material to have a gel time of less than 120 seconds as measured by a gel time measurement”; “a first biocompatible precursor”; “a second biocompatible precursor”; “the first biocompatible precursor”; “the second biocompatible precursor”; “resistant to enzymatic degradation”; “one isolated hydrolytically degradable ester group”; “mixing at least the first biocompatible precursor and the second biocompatible precursor in situ to form a device comprising a crosslinked hydrogel”; “covalent bonds formed by reaction of the functional groups of the first biocompatible precursor and second biocompatible precursor with each other and further comprising”; “wherein the crosslinked hydrogel”; “degradable by hydrolysis of the at least one isolated hydrolytically degradable ester group”; “the second biocompatible precursor has a molecular weight of less than about 2000”; “the second precursor is a member of the group consisting of ornithine, spermine, spermidine, urea, guanidine, dianmipimelic acid, diaminobutyric acid, methylornithine, diaminopropionic acid, cystine, lanthionine, cystamine, trioxatridecanediamine, cyclohexanebis(methylamine), tetraethylenepentamine,

pentaethylenehexamine, methylenebis(methylcyclohexamine), diaminocyclohexane, n-(2-aminoethyl)-1,3-propanediamine, diaminomethyldipropylamine, iminobispropylamine, bis(hexamethylene)triamine, triethylenetetramine, bis(aminopropyl)ethylenediamine, bis(2-aminoethyl)-1,3-propanediamine, bis(aminopropyl)propanediamine, diamniomethylpropane, 1,2-diamino-2-methylpropane, 1,3-diaminopentane, dimethylpropanediamine, 2,2-dimethyl 1,3-propanediamine, methylpentanediamine, 2-methyl-1, 5 pentanediamine, diaminoheptane, diaminooctane, diaminononane, and diaminododecane”; “a third biocompatible precursor”; “the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor are reactable with each other to form a crosslinked hydrogel”; “the first, second, or third biocompatible precursors”; “isolated hydrolytically degradable ester group”; “the applicator is configured to mix at least the first precursor, the second precursor, and the third precursor to form a crosslinked hydrogel in situ comprising”; “covalent bonds formed by reaction of the functional groups of the precursors”; “a sufficient number of the at least one isolated hydrolytically degradable ester groups in the crosslinked hydrogel so that the crosslinked hydrogel is degradable in less than about 180 days”; “about 180 days”; “the second biocompatible precursor and the third biocompatible precursor each have a molecular weight of less than about 1000”; “about 90”; “the first, the second, and the third biocompatible precursors are resistant to enzymatic degradation”; “mixing, in situ, the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor to form a crosslinked hydrogel that comprises”; “covalent bonds formed by reaction of the functional groups of the first, the second, and the third biocompatible precursors”; “a sufficient number”; “isolated”; “the second biocompatible precursor is a member of the group consisting of tetraethylenepentamine, pentaethylenehexamine, methylenebis(methylcyclohexamine), diaminocyclohexane, n-(2-

aminoethyl)- 1,3 -propanediamine, diaminomethyldipropylamine, and iminobispropylamine”; “identifying a medical condition”; “mixing a first precursor with”; “a second precursor in situ”; “the first biocompatible synthetic hydrophilic polymer precursor”; “the second biocompatible synthetic hydrophilic polymer precursor”; “the first precursor is selected have only one or two chemically hydrolytically degradable ester bonds per every electrophilic functional group on the first precursor”; “the second precursor comprises at least three nucleophilic functional groups”; “the biodegradable groups of the hydrogel consist of the esters”; “essentially fully degradable”; “mixing the first and the second synthetic hydrophilic polymer precursors”; “essentially every ester bond in the hydrogel is separated from other ester bonds in the hydrogel by at least three covalent bonds when the hydrogel is formed”; “the medical condition is wound covering”; “the medical condition is tissue sealing”; “the medical condition is tissue coating”; “the second precursor has a molecular weight of less than about 1000 Daltons”; “one of the precursors is selected to further comprise a chemical group having the formula $(CH_2CH_2O)_n$ ”.

II. The Asserted Claims Are Invalid Under 35 U.S.C. § 102 For Anticipation And/Or 35 U.S.C. § 103 For Obviousness

All of the Asserted Claims are invalid under 35 U.S.C. §§ 102 and/or 103 for anticipation and/or obviousness.

A. Legal Standards

1. Anticipation

“A patent is invalid for anticipation if a single prior art reference discloses each and every limitation of the claimed invention.” *Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003). “Anticipation does not require the actual creation or reduction to practice of the prior art subject matter; anticipation requires only an enabling disclosure,” that is, an

anticipatory reference “need only enable subject matter that falls within the scope of the claims at issue, nothing more.” *Id.* at 1380-81.

“[A] prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference.” *Id.* at 1377. The doctrine of inherent anticipation enforces the basic principle that the public “remains free to make, use or sell prior art compositions or processes, regardless of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate.” *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1348 (Fed. Cir. 1999).

Inherent anticipation of a patent requires only that “the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the claimed product.” *SmithKline* 403 F.3d at 1343. Inherent anticipation does not require that the missing characteristic always occurs under all conceivable conditions, but only requires that the result “necessarily and inevitably forms ... under normal conditions.” *Schering*, 339 F.3d at 1378. Lack of inherent anticipation cannot be shown by methods employing “extraordinary measures.” *SmithKline*, 403 F.3d at 1343-44.

Inherent anticipation “does not require a person of ordinary skill in the art to recognize the inherent disclosure in the prior art at the time the prior art is created.” *Schering*, 339 F.3d at 1377. In addition, “an insufficient scientific understanding does not defeat a showing of inherency.” *Atlas Powder Co.*, 190 F.3d at 1349.

“[I]f the PTO did not have all the material facts before it, its considered judgment may lose significant force. And, concomitantly, the challenger’s burden to persuade the jury of its

invalidity defense by clear and convincing evidence may be easier to sustain.” *i4i*, 131 S. Ct. at 2251 (internal citations omitted).

2. Obviousness

Section 103 states that “[a] patent may not be obtained through the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” 35 U.S.C. § 103(a); *Tokai Corp. v. Easton Enterprises, Inc.*, 632 F.3d 1358, 1366 (Fed. Cir. 2011).

In assessing obviousness under section 103, “the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved.” *KSR*, 550 U.S. at 406. The hypothetical “person of ordinary skill in the art” is attributed “knowledge of all prior art in the field of the inventor’s endeavor and of prior art solutions for a common problem even if outside that field.” *In re Nilssen*, 851 F.2d 1401, 1403 (Fed. Cir. 1988). “Whether a claimed invention is unpatentable as obvious ... is a question of law based on underlying findings of fact.” *Okajima v. Bourdeau*, 261 F.3d 1350, 1354 (Fed. Cir. 2001).

Obviousness may be shown based on a combination of references or based on a single reference. *Boston Scientific Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982, 989-990 (Fed. Cir. 2009). The “reason, suggestion or motivation to combine may be found explicitly or implicitly: 1) in the prior art references themselves; 2) in the knowledge of those of ordinary skill in the art that certain references, or disclosures in those references, are of special interest or importance in the field; or 3) from the nature of the problem to be solved. . . .” *Ruiz v. A.B. Chance Co.*, 234 F.3d 654, 665 (Fed. Cir. 2000.) The motivation to combine is not subject to a rigid formula,

such that it is also relevant where “common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not.” *Leapfrog Enters. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1161 (Fed. Cir.2007). The flexible nature of the obviousness inquiry allows consideration of information including market forces; design incentives; and the “interrelated teachings of multiple patents.” *KSR*, 550 U.S. at 418-21. “Under the correct analysis, any need or problem known in the field of endeavor at the time of the invention and addressed by the patent [or application at issue] can provide a reason for combining the elements in the manner claimed.” *Id.* at 420. “[I]f a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.” *Id.* Art is analogous if it is either from the same “field of endeavor” or, even if outside the field of endeavor, “is reasonably pertinent to the [particular] problem with which the inventor [is involved].” *In re Kahn*, 441 F.3d 977, 986-87 (Fed. Cir. 2006). “[*KSR*] directs us to construe the scope of analogous art broadly.” *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1238 (Fed. Cir. 2010).

A patent claim is obvious when it does no more than combine familiar elements according to known methods to yield predictable results. *KSR*, 550 U.S. at 415-17 (“If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.”); *Wm. Wrigley Jr. Co. v. Cadbury Adams*, 683 F.3d 1356, 1362-63 (Fed. Cir. 2012); *Tyco Healthcare Group LP v. Mutual Pharm. Co., Inc.*, 642 F.3d 1370, 1377 (Fed. Cir. 2011); *Tokai*, 632 F.3d at 1366. “Common sense teaches ... that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill would be able to fit the teachings of multiple patents together like pieces of a puzzle.” *KSR*, 550 U.S. at 420. “When there is a

design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. *Id.* at 421. When this leads to the anticipated success, “it is likely the product not of innovation but of ordinary skill and common sense.” *Id.*

“The patentee bears the burden of showing that a nexus exists between the claimed features of the invention and the objective evidence offered to show non-obviousness.” *WMS Gaming, Inc. v. Int’l Game Tech.*, 184 F.3d 1339, 1359 (Fed. Cir. 1999). As an example, “[e]vidence of commercial success, or other secondary considerations, is only significant if there is a nexus between the claimed invention and the commercial success Thus, if the commercial success is due to an unclaimed feature of the device, the commercial success is irrelevant. So too if the feature that creates the commercial success was known in the prior art, the success is not pertinent.” *Ormco Corp. v. Align Tech., Inc.*, 463 F.3d 1299, 1311-12 (Fed. Cir. 2006). Near-simultaneous invention provides evidence that the claimed invention is obvious. *See Ecolchem, Inc. v. S. California Edison Co.*, 227 F.3d 1361, 1379 (Fed. Cir. 2000); *The Int’l Glass Co. v. United States*, 187 Ct.Cl. 376, 408 F.2d 395, 405 (1969).

A strong case of obviousness cannot be overcome by secondary considerations. *Leapfrog Enters., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007); *Agrizap, Inc. v. Woodstream Corp.*, 520 F.3d 1337, 1344 (Fed. Cir. 2008); *Muniauction*, 532 F.3d at 1323. The existence of secondary considerations “does not control the obviousness determination.” *Richardson-Vicks Inc. v. Upjohn Co.*, 122 F.3d 1476, 1483 (Fed. Cir. 1997).

B. Priority Dates are at Issue for all Asserted Claims

The ’034 patent was filed as a continuation-in-part on November 9, 2001, which is the presumptive priority date. It is Plaintiffs’ burden to establish that all of the elements of any asserted claim of the ’034 patent have both written description and enablement support in the

pre-November 9, 2001 application(s) should it seek to predate November 9, 2001 for purposes of the prior art.

The '418 patent is a continuation of the '566 patent, which was filed as a continuation of the '034 patent, which is itself a continuation-in-part application filed on November 9, 2001, which is the presumptive priority date. It is Plaintiffs' burden to establish that all of the elements of any asserted claim of the '418 patent have both written description and enablement support in the pre-November 9, 2001 application(s) should it seek to predate November 9, 2001 for purposes of prior art.

The '566 patent was filed as a continuation of the '034 patent, which is itself a continuation-in-part application filed on November 9, 2001, which is the presumptive priority date. It is Plaintiffs' burden to establish that all of the elements of any asserted claim of the '566 patent have both written description and enablement support in the pre-November 9, 2001 application(s) should it seek to predate November 9, 2001 for purposes of the prior art.

The '406 patent was filed December 3, 1999, which is the presumptive priority date. It is Plaintiffs' burden to establish that all of the elements of any asserted claim of the '406 patent have both written description and enablement support in the pre-December 3, 1999 application(s) should it seek to predate December 3, 1999 for purposes of prior art.

The '3,705 patent was filed as a continuation-in-part on May 29, 2008, which is the presumptive priority date. It is Plaintiffs' burden to establish that all of the elements of any asserted claim of the '3,705 patent have both written description and enablement support in the pre-May 29, 2008 application(s) should it seek to predate May 29, 2008 for purposes of prior art.

The '5,705 patent was filed as a division of an abandoned application that was a continuation of the '406 patent filed on December 3, 1999, which is the presumptive priority

date. It is Plaintiffs' burden to establish that all of the elements of any asserted claim of the '5,705 patent have both written description and enablement support in the pre-December 3, 1999 application(s) should it seek to predate December 3, 1999 for purposes of prior art.

Identification of prior art by HyperBranch has put the priority date at issue for all of the Asserted Claims, including references with prior art status under 35 U.S.C. §§ 102(a), 102(b), and 102(e). Lack of priority for the Asserted Claims is also supported by the proper inventorship of each of the individual claims, such as demonstrated by the testimony of Sawhney and Bennett that demonstrates that the inventions were conceived and reduced to practice by individuals who have admitted to their contribution to the conception of the claimed inventions long after the initial filing of any provisional applications.

C. The Asserted Claims are Invalid Under 35 U.S.C. § 102 for Anticipation and/or 35 U.S.C. § 103 for Obviousness

At least the following references, each of which constitutes prior art to the Asserted Patents at least pursuant to 35 U.S.C. §§ 102(a), (b) and/or (e), and/or evidences the state of the prior art, alone or in combination, render the Asserted Claims of the Asserted Patents invalid due to anticipation under 35 U.S.C. § 102 and/or obviousness under 35 U.S.C. § 103: US 2,533,004; US 3,520,949; US 4,101,380; US 4,414,976; US 4,359,049; US 4,565,784; US 4,427,651; US 4,631,188; US 4,693,887; US 4,631,055; US 4,601,286; US 4,735,616; US 4,740,534; US 4,717,378; US 5,160,745; US 4,646,730; EP 0246380; EP 0246380; US 4,803,075; US 4,979,959; US 4,932,942; US 4,826,945; US 4,937,270; US 4,978,336; US 4,874,368; US 5,281,662; US 4,902,281; US 4,925,677; US 5,041,292; US 4,938,763; US 5,278,202; US 4,938,763; US 5,733,950; US 5,681,576; US 5,550,188; US 5,800,541; US 5,565,519; US 5,550,187; US 5,162,430; US 5,643,464; US 5,614,587; US 5,527,856; US 5,470,911; US 5,475,052; US 5,744,545; US 5,786,421; US 5,446,091; US 5,413,791; US 5,304,595; US

5,328,955; US 5,324,775; US 5,936,035; EP 0414848; US 5,100,992; US 5,405,607; US 5,776,493; US 5,869,096; US 5,104,909; US 5,213,808; US 5,116,315; US 5,093,319; WO 1991/009641; US 5,318,524; US 5,030,215; US 5,219,564; US 5,455,027; US 5,399,351; US 5,645,583; US 5,292,362; US 5,741,223; US 5,410,016; US 5,529,914; US 5,143,662; US 5,290,776; US 5,296,518; US 6,020,326; US 5,605,938; US 5,330,768; US 5,587,175; US 5,368,563; US 5,192,743; US 5,213,760; US 5,567,435; US 6,306,922; US 5,986 043; US 5,626,863; US 5,801,033; Larwood & Szoka, J. Labelled Compounds and Radiopharmaceuticals. V. XXI, No. 7 (1984) p.603; Mei et al. Nanoscale Res. Lett. (2009) 4: 1530-1539; Pathak et al. J. Am. Chem. Soc., 114 (1992) pp.8311-8312; Sawhney et al., Macromolecules, (1993) 26, 581-587; Ulbrich et al. Makromol. Chem. 187 (1986) 1131-1144; Veronese et al. Applied Biochem. And Biotechnol. Vol 11 (1985) p. 141; Principles of Color Technology, Roy S. Burns, 2000, Wiley & Sons; Epstein. The Spine Journal. 10 (2010) 1065-1068; Zhao & Harris, Journal of Pharmaceutical Sciences, (1998) Volume 87, Issue 11, pages 1450–1458, November; Davis & Cordeaux. “Tissue Adhesive: use and application.” *Emergency Nurse*. 2(2) 1994. pp. 16-18; US 6,465,001; US 5,858,746; US 5,573,934; US 5,514,379; US 5,618,563; US 5,844,023; US 5,426,148; US 5,814,621; US 5,395,923; US 5,749,968; US 5,476,909; US 5,505,704; US 5,431,639; US 5,773,025; US 5,446,090; US 5,423,821; US 5,807,581; US 5,668,236; US 5,474,540; US 5,672,622; US 5,631,322; US 5,514,380; US 5,419,491; US 5,583,114; WO 1996/003159; WO 1996/014095; 2014/0243428; 2006/0062768; US 4,839,345; US 6,371,975; US 6,458,147; US 4,162,162; US 5,475,052; US 5,292,362; US 5,328,955; US 7,279,176; US 6,162,241; US 5,719,031; US 6,165,201; CA 1054517; WO 95/34605; WO 2000/09087; WO 97/22371; WO 2000/033764; US 6,165,489; US 5,605,541; US 5,810,885; US 5,932,462; US 5,698,213; US 5,962,023; US 6,261,544; EP 0732109; US 5,580,923; US 5,612,052; US

5,714,159; US 5,656,035; US 6,033,654; US 6,129,761; US 6,124,273; US 6,201,065; US 5,830,196; US 2001/0003126; US 6,323,278; WO 1997/019973; EP 0863933; US 6,174,645; US 5,990,193; US 6,051,648; WO 1997/022372; US 5,752,974; US 6,458,889; US 6,166,130; WO 1997/022371; US 5,874,500; US 6,428,571; US 5,702,361; US 5,900,245; US 6,051,248; US 6,136,333; US 2004/0076602; US 2008/0287633; US 6,177,095; US 7,332,566; US 7,009,034; US 6,214,966; US 5,830,178; US 5,863,551; US 6,413,539; US 6,258,351; WO 1998/035631; US 6,271,278; US 6,017,301; US 6,133,325; US 6,153,211; US 6,162,241; WO 99/08718; WO 1999/008718; WO1999/010022; WO 1999/014259; US 6,149,931; WO 1999/022770; WO 1999/034833; US 6,156,345; US 6,251,382; US 6,156,531; US 6,818,018; WO 2000/009087; US 6,632,457; US 6,371,975; US 6,458,147; US 6,110,484; US 6,277,394; WO 2000/033764; US 2008/0095736; US 6,566,406; US 6,958,212; US 6,312,725; US 6,495,127; US 6,238,403; US 6,348,558; US 6,515,534; WO 2001/066017; WO 2001/068155; US 6,303,102; US 6,610,033; EP 1967220; JP 3-502704; JP 5-508161; JP 6-508169; JP 10-503102; WO 89/02445; WO 92/00105; WO 92/20349; WO 99/03454; Achterberg et al., "Hydroactive Dressings and Serum Proteins: An In Vitro Study," J Wound Care, 5:79-82 (1996)(abstract); Audebert MD, "Initial Bordeaux Experience with SprayGel Adhesion Barrier System", Presented at the 10th Congress of the European Society for Gynaecological Endoscopy, Nov. 21-24, 20001, Lisbon, Portugal; Baines et al., "Adsorption and Removal of Protein Bound to Hydrogel Contact Lenses," Optom Vis Sci 67:807-810 (1990); Bick, "Hemostasis Defects," Seminars in Thrombosis and Hemostasis 11:263-264 (1985); Bick, "Physiology and Pathophysiology of Hemostasis During Cardiac Surgery" (excerpts), (1995); Bite et al., "Macrosorb Kieselguhr-Agarose Composite Adsorbents. New Tools for Downstream Process Design and Scale Up. Scientific Note," App/ Biochem Biotechno/ 18:275-284 (1988); Brochure information related to

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Fleischmann et al. *Polymers* (2015) v. 7; 717-746; Fortier et al. *Biotechnol. Appl. Biochem.* 17 (1993) p.115-130.

The chart attached as Appendix A is provided in support of HyperBranch's 35 U.S.C. § 102 and 35 U.S.C. § 103 contentions. The chart addresses each element of the Asserted Claims, and identifies representative, non-exhaustive disclosures from the references listed above. Such references can be combined with any other applicable reference to render the claims obvious under 35 U.S.C. § 103. The identified references generally deal with at least one of the following areas: polymer (including hydrogel) technology, tissue sealant technology, or visualization agents and/or colorants used in medical devices. For example, several prior art references are found within the same general field of applying polymeric materials to tissues. In particular, the use of a color additive to facilitate visualization and assessment of polymer thickness was known for specific use with dural sealants. These references would have been within the knowledge of a person of ordinary skill in the art familiar with polymers, hydrogel, and/or medical materials. A person of ordinary skill in the art would have been motivated to combine any of these prior art references to arrive at the claimed inventions with a reasonable expectation of success, thereby rendering the Asserted Claims invalid under 35 U.S.C. § 103.

The appended chart indicates, for each element of the Asserted Claims, at least one location in a cited prior art reference at which the limitations of a given claim element may be found. The chart does not necessarily indicate every location within the particular prior art reference at which the given claim element may be found. Thus, when considering a citation provided to a particular prior art reference for a given claim element, the following points should be noted:

- a. Citations to a particular structure or set of structures in a given figure should be understood as also referring to all identical, parallel, correlating, or corresponding structures or sets of structures in other figures in the reference or in the text of the reference. Such citations should further be understood as referring to any alternative embodiments disclosed in the reference for the cited structure or sets of structures.
- b. Citations to a particular structure or set of structures in a given figure should be understood as also referring to the text in the reference that describes, explains, or elucidates upon the cited structure(s) or the given figure.
- c. Citations to text in a reference should be understood as also referring to any figures, structures, or embodiments described therein.
- d. The fact that certain entries in the charts may include citations to multiple alternative structures in a prior art reference should not be construed to mean that for the references for which only a single citation is provided, the above points do not apply. Further, the fact that certain sections or pages of a prior art reference are cited for a given claim element should not be construed to mean that other sections or pages do not contain additional disclosure or description reading on the same claim element. The above points are applicable to all entries in the appended chart.

The analysis contained in the appended chart does not necessarily reflect the construction that HyperBranch believes ought to be given to the asserted claims. This analysis instead reflects HyperBranch's understanding of Plaintiffs' interpretation of the asserted claims, as reflected in

Plaintiffs' September 30, 2016 Preliminary Infringement Contentions. Even under a proper construction, the claims are still invalid in light of the prior art.

HyperBranch also incorporates by reference its Petition for *Inter Partes* Review of the '034 patent filed with the U.S. Patent and Trademark Office on September 16, 2016 (IPR2016-01836).

III. The Asserted Claims Of The '3,705 And '5,705 Patents Are Invalid For Obviousness-Type Double Patenting

A. Legal Standard

"[I]t is a bedrock principle of our patent system that when a patent expires, the public is free to use not only the same invention claimed in the expired patent but also obvious or patentably indistinct modifications of that invention." *Gilead Sciences Inc. v. Natco Pharma Ltd.*, 753 F.3d 1208, 1214 (Fed. Cir. 2014). "And that principle is violated when a patent expires and the public is nevertheless barred from practicing obvious modifications of the invention claimed in that patent because the inventor holds another later-expiring patent with claims for obvious modifications of the invention." *Id.*

B. The Asserted Claims of the '3,705 and '5,705 Patents are Invalid for Obviousness-Type Double Patenting

The claims of the '3,705 and '5,705 patents are invalid for obviousness-type double patenting. Plaintiffs have numerous patents and hundreds of claims (including 105 Asserted Claims) allegedly covering the same subject matter. These patents, as well as other co-owned patents, that are indicative of invalidity for obviousness-type double patenting include at least U.S. Patent Nos. 6,566,406; 7,009,034; 7,332,566; 7,592,418; 8,003,705; 8,535,705; 7,347,850; 7,057,019; 6,887,974; 7,211,651; 7,605,232; 8,557,535; and 6,514,534. The later-expiring claims of the '3,705 and '5,705 patents are invalid because the differences in the subject matter of the claims do not render them patentably distinct, and they are not protected from invalidity

for double patenting by the 35 U.S.C. § 121 safe harbor. Invalidity for double patenting is further demonstrated by the extensive overlap in claimed subject matter across the Asserted Claims, as shown in the chart at Appendix A.

IV. The Asserted Claims Are Invalid Under 35 U.S.C. § 101

A. Legal Standard for Patentable Subject Matter

Section 101 states “[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor.” 35 U.S.C. § 101. “Laws of nature, natural phenomena, and abstract ideas” are not patentable subject matter under § 101. *Alice Corp. Pty. Ltd. v. CLS Bank Int’l*, 134 S. Ct. 2347, 2354 (2014). These are “the basic scientific tools of scientific and technological work.” *Id.* “We have described the concern that drives this exclusionary principle as one of pre-emption.” *Id.* The Supreme Court has “repeatedly emphasized this...concern that patent law not inhibit further discovery by improperly tying up the future use of these building blocks of human ingenuity.” *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (2012). In determining whether a claim is patent-eligible, under § 101, courts must “distinguish between patents that claim the ‘building blocks’ of human ingenuity and those that integrate the building blocks into something more.” *Alice*, 134 S. Ct. at 2354 (internal citations and quotations omitted).

B. The Asserted Claims are Invalid Under 35 U.S.C. § 101

Plaintiffs contend that “the visualization agent is also met by the air bubbles in the hydrogel generated by the applicator for the Adherus AutoSpray Dural Sealant.” *See, e.g.*, Plaintiffs’ Preliminary Infringement Contentions, dated September 30, 2016. Plaintiffs thus contend that the Asserted Claims cover the natural phenomenon of bubbles being entrained in a

material and/or that air itself can be the claimed visualization agent. The Asserted Claims therefore cover non-patentable subject matter, and are invalid under § 101.

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CERTIFICATE OF SERVICE

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APPENDIX A

Claim element	Patents in which element is found	Relevant Prior Art References
A method of preparing a Composition		
A method of preparing a composition suitable to coat a tissue of a patient or treat a medical condition	[7,009,034, c1]: A method of preparing a composition suitable to coat a tissue of a patient, the method comprising: [7,009,034, c16]: A method for formulating a polymer composition that crosslinks to form a hydrogel, [7,332,566, c1]: A polymeric coating for a substrate comprising: [8,535,705, c1]: A method of making a biocompatible degradable hydrogel to treat a medical condition of a patient comprising:	<ul style="list-style-type: none">• <u>Gayet & Fortier, J. Contr. Rel. 38 (1996) 177-184:</u> [Col. 1 p. 177] “Since [hydrogels] are used in many applications such as artificial cells and organs, biomaterials or contact lenses” We believe that this family of BSA-PEG hydrogels could be useful for the preparation of controlled release devices in the field of wound dressing.• <u>Prestwich et al., JACS 1994, 116 p.7515. p.7521:</u> col. 2: The highly porous three-dimensional structures of the HA hydrogels suggest that they may be appropriate biodegradable scaffolds for the adherence and growth of cells in three dimensions.• <u>US 5,583,114:</u> Col. 2 (Summary): The present invention is a nontoxic, absorbable adhesive sealant composition which may be used to bond and/or seal tissue.• <u>WO 00/09087:</u> These and other objects of the present invention are accomplished in accordance with the principles of the present invention by providing methods of using hydrogels to form regional barriers in situ to prevent the formation of post-surgical adhesions. The regional hydrogel layers of the present invention also may be used to deliver drugs or other therapeutic agents to the region of interest, typically a body cavity.• <u>WO 2000/033764:</u> Another object of this invention is to provide methods for preparing tissue conforming, biocompatible crosslinked polymers in a desirable form, size and shape. Another object of this invention is to provide methods for using biocompatible crosslinked polymers to form medically useful devices or implants for use as surgical adhesion prevention barriers, as implantable wound dressings, as scaffolds for cellular growth for tissue engineering, or as surgical tissue adhesives or sealants .• <u>Tse:</u> Butyl-2-cyanoacrylate tissue adhesive successfully sealed three cases of CSF leaks encountered during orbital surgery. The application of tissue adhesive was followed by prompt cessation of the leak.• <u>US 5,614,587 (Rhee):</u> This invention relates generally to compositions useful as biological or surgical adhesives; more specifically, it relates to bioadhesive compositions comprising collagen crosslinked using a multifunctionally activated synthetic hydrophilic polymer, as well as methods of using such compositions to

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>effect adhesion between a first surface and a second surface, wherein at least one of the first and second surfaces is preferably a native tissue surface.</p> <ul style="list-style-type: none">• <u>2014/0243428</u>: The disclosure provides for self-healing hydrogels, complex structures made therefrom, and use thereof, including use of the hydrogels as self-healing coatings, self-healing sealants, tissue adhesives, and drug carriers.• <u>4,839,345</u>: This invention relates to hydrated adhesive gels, especially hydrated adhesive gels for a self-adhesion cataplasms and patch agents having sheet shape.• <u>5,328,955</u>: The dehydrated, solid object can be ground into particles which can be suspended in a non-aqueous fluid such as an oil and injected into a living being for the purpose of providing soft tissue augmentation.• <u>6,165,201</u>: Methods and apparatus of forming in situ tissue adherent barriers are provided using a sprayer capable of applying two or more viscous crosslinkable solutions to tissue.• <u>WO 95/34605</u>: this invention relates to the manufacture of tinted hydrogel materials, such as contact lenses, wherein the tint is achieved by use of vat dyes.• <u>Champagne</u>: Clinically proven, the toxic degradation products of longer-chain cyanoacrylates are barely detectable on extraction studies, such that they are widely considered non-toxic.• <u>Ellis & Shaikh</u>: Fibrin glue, since the early 1970s, has gained popularity as a biologic adhesive amount the surgical specialties, and has been reported to be a safe bioadhesive and sealant ... We have been using histoacryl glue for closure of surgical incisions in facial and plastic reconstructive surgery.• <u>Pathak, J.A.C.S. 1992, 114, 8311-8312</u>: Here we report the synthesis of stable, biocompatible gels with permselectivity appropriate for immunoprotection via rapid photopolymerization of water-soluble poly (ethylene glycol)-based macromers in direct contact with cells and tissue without cytotoxicity.• <u>Sawhney et al., Macromolecules, (1993) 26, 581-587</u>: Macromers having a poly(ethylene glycol) central block, extended with oligomers of α-hydroxy acids such as oligo(d,l-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>of cross-linked gels. These gels degrade upon hydrolysis of the oligo(a-hydroxy acid) regions into poly(ethylene glycol), the a-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular drug delivery.</p> <ul style="list-style-type: none">• <u>WO 2000/09087</u>: It is another object of this invention to provide in situ formation of regional barriers by macromere solutions at concentrations close to equilibrium hydration levels, to reduce or prevent post-surgical adhesion formation.• <u>WO 2000/033764</u>: Biocompatible crosslinked polymers, and methods for their preparation and use, are disclosed in which the biocompatible crosslinked polymers are formed from water soluble precursors having electrophilic and nucleophilic groups capable of reacting and crosslinking in situ. Methods for making the resulting biocompatible crosslinked polymers biodegradable or not are provided, as are methods for controlling the rate of degradation. The crosslinking reactions may be carried out in situ on organs or tissues or outside the body. Applications for such biocompatible crosslinked polymers and their precursors include controlled delivery of drugs, prevention of post-operative adhesions, coating of medical devices such as vascular grafts, wound dressings and surgical sealants.• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>5,292,362</u>: The present invention is directed to a composition adapted to bond separated tissues together or to coat tissues or prosthetic materials to enhance strength and water tightness preferably upon the application of energy and particularly to a composition which is activated by a laser to form a strong, biologically compatible bond or coating.• <u>Zhao</u>: Hydrogels are generally considered as biocompatible materials because of their high water content. They have been used in a variety of biomaterial and

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>biotechnology applications, such as tissue engineering, artificial organs, and drug delivery.</p> <ul style="list-style-type: none">• <u>Davis</u>: One product widely used in A&E departments contains a non-toxic blue dye which enables visualisation of the quantity applied. Surgical glue may be used as an alternative, or adjunct to more traditional methods of wound closure, such as sutures, staples, and wound closure ships.• <u>7,279,176</u>: Hydrogels releasing or producing NO, most preferably photopolymerizable biodegradable hydrogels capable of releasing physiological amounts of NO for prolonged periods of time, are applied to sites on or in a patient in need of treatment thereof for disorders such as restenosis, thrombosis, asthma, wound healing, arthritis, penile erectile dysfunction or other conditions where NO plays a significant role.• <u>6,162,241</u>: A method of controlling hemostasis by applying a hemostatic agent in a tissue sealant composition. The tissue sealant is a biodegradable, biocompatible synthetic polymer that may not intrinsically possess strong hemostatic properties.• <u>WO 97/22371</u>: Also disclosed are methods for using the crosslinked polymer compositions to effect adhesion between a first surface and a second surface; to effect tissue augmentation; to prevent the formation of surgical adhesions; and to coat a surface of a synthetic implant.• <u>6,371,975</u>: A biocompatible and biodegradable barrier material is applied to a tissue region, e.g., to seal a vascular puncture site. The barrier material comprises a compound, which is chemically cross-linked without use of an enzyme to form a non-liquid mechanical matrix. The compound preferably includes a protein comprising recombinant or natural serum albumin, which is mixed with a polymer that comprises poly(ethylene) glycol (PEG), and, most preferably, a multi-armed PEG polymer.• <u>6,458,147</u>: A biocompatible and biodegradable hydrogel compound, which is free of a hemostatic agent, is applied to arrest the flow of blood or fluid from body tissue. The compound preferably includes a protein comprising recombinant or natural serum albumin, which is mixed with a polymer that comprises poly(ethylene) glycol (PEG), and, most preferably, a multi-armed PEG polymer.• <u>Bouhadir et al</u>: we have synthesized new polymers derived from sodium

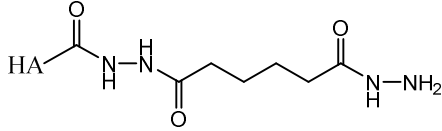
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>poly(guluronate), the portion of the alginate molecule that is responsible for its gelling behavior. In many approaches to engineer tissues, it is desirable to utilize a biodegradable polymer as the cell transplantation matrix ... new biomaterials derived from alginate that are biodegradable, possess a wide range of physical and mechanical properties, and exhibit the potential for improved cellular interaction.</p> <ul style="list-style-type: none"> • <u>Otani</u>: In this study, a rapidly curable hydrogel glue was prepared as the seal for lung air leak. Mixing an aqueous solution of gelatin and poly(l-glutamic acid) with a water soluble carbodiimide produced a hydrogel. The mixed gelatin and PLGA aqueous solution sets in several seconds to a hydrogel at 37 °C with the addition of WSC; this is as short as conventional fibrin glue.
Hydrogel is formed in situ	<p>[8,003,705, c1]: mixing at least the first biocompatible precursor and the second biocompatible precursor in situ to form a device comprising a crosslinked hydrogel that comprises covalent bonds formed by reaction of the functional groups of the first biocompatible precursor and second biocompatible precursor with each other and further comprising the at least one isolated hydrolytically degradable ester group; wherein the crosslinked hydrogel is resistant to enzymatic degradation, is degradable by hydrolysis of the at least one isolated hydrolytically degradable ester group so that the device is degradable in less than about 180 days,</p> <p>[8,003,705, c11]: mixing, in situ, the first biocompatible precursor, the second biocompatible precursor, and the third biocompatible precursor to form a crosslinked hydrogel that comprises covalent bonds formed by reaction of the functional groups of the first, the second, and the third biocompatible precursors, with the hydrogel being resistant to enzymatic degradation and comprising the at least one isolated hydrolytically degradable ester group;</p>	<ul style="list-style-type: none"> • <u>Tse</u>: Butyl-2-cyanoacrylate tissue adhesive successfully sealed three cases of CSF leaks encountered during orbital surgery. The application of tissue adhesive was followed by prompt cessation of the leak. • <u>US 5,614,587 (Rhee)</u>: In a general method for effecting the attachment of a first surface to a second surface, collagen and a multifunctionally activated synthetic hydrophilic polymer are mixed to initiate crosslinking, the collagen--synthetic polymer mixture is applied to a first surface before substantial crosslinking has occurred between the collagen and the synthetic polymer, then a second surface is brought into contact with the first surface. At least one of the first and second surfaces is preferably a native tissue surface. • <u>Gayet & Fortier, J. Contr. Rel. 38 (1996) 177-184</u>: We believe that this family of BSA-PEG hydrogels could be useful for the preparation of controlled release devices in the field of wound dressing. • <u>Prestwich et al.</u>: The highly porous three-dimensional structures of the HA hydrogels suggest that they may be appropriate biodegradable scaffolds for the adherence and growth of cells in three dimensions. And as potential treatment of osteoarthritis and rheumatoid arthritis. • <u>2014/0243428</u>: Figure 10E. Adhesion of A6ACA hydrogels to rabbit gastric mucosa. • <u>6,371,975</u>: FIG. 20 is the non-liquid barrier network formed after the liquid barrier material cross-links in situ in tissue to seal the vascular puncture site; • <u>5,328,955</u>: The method can be varied so that the reaction between the collagen

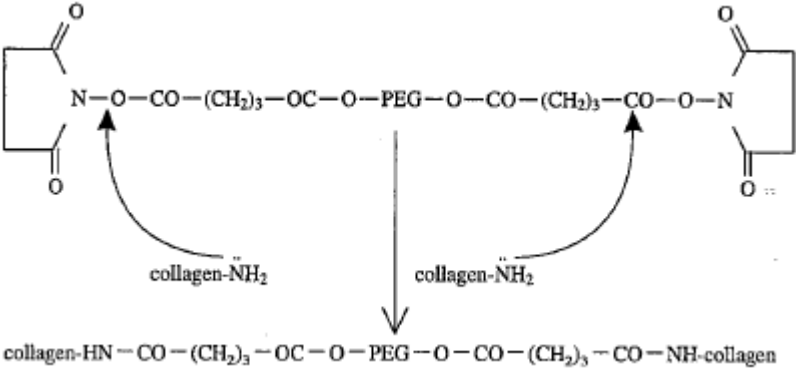
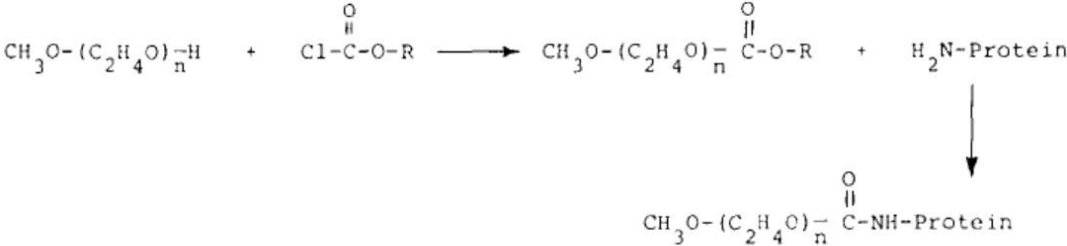
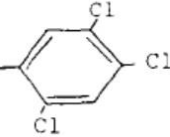
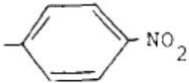
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>and the polymer occurs in situ. Example 4 gives in situ crosslinking.</p> <ul style="list-style-type: none">• <u>6,165,201</u>: Methods and apparatus of forming in situ tissue adherent barriers are provided using a sprayer capable of applying two or more viscous crosslinkable solutions to tissue.• <u>Ellis & Shaikh</u>: Fibrin glue, since the early 1970s, has gained popularity as a biologic adhesive amount the surgical specialties, and has been reported to be a safe bioadhesive and sealant ... We have been using histoacryl glue for closure of surgical incisions in facial and plastic reconstructive surgery ... the tissues to be approximated should be as dry as possible.• <u>Pathak, J.A.C.S. 1992, 114, 8311-8312</u>: Here we report the synthesis of stable, biocompatible gels with permselectivity appropriate for immunoprotection via rapid photopolymerization of water-soluble poly (ethylene glycol)-based macromers in direct contact with cells and tissue without cytotoxicity.• <u>Sawhney et al., Macromolecules, (1993) 26, 581-587</u>: Macromers having a poly(ethylene glycol) central block, extended with oligomers of a-hydroxy acids such as oligo(dl-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation of cross-linked gels. These gels degrade upon hydrolysis of the oligo(a-hydroxy acid) regions into poly(ethylene glycol), the a-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular drug delivery.• <u>WO 2000/09087</u>: It is another object of this invention to provide in situ formation of regional barriers by macromere solutions at concentrations close to equilibrium hydration levels, to reduce or prevent post-surgical adhesion formation.• <u>WO 2000/033764</u>: Biocompatible crosslinked polymers, and methods for their preparation and use, are disclosed in which the biocompatible crosslinked polymers are formed from water soluble precursors having electrophilic and nucleophilic groups capable of reacting and crosslinking in situ. Methods for

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>making the resulting biocompatible crosslinked polymers biodegradable or not are provided, as are methods for controlling the rate of degradation. The crosslinking reactions may be carried out in situ on organs or tissues or outside the body. Applications for such biocompatible crosslinked polymers and their precursors include controlled delivery of drugs, prevention of post-operative adhesions, coating of medical devices such as vascular grafts, wound dressings and surgical sealants.</p> <ul style="list-style-type: none">• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>5,292,362</u>: The present invention is directed to a composition adapted to bond separated tissues together or to coat tissues or prosthetic materials to enhance strength and water tightness preferably upon the application of energy and particularly to a composition which is activated by a laser to form a strong, biologically compatible bond or coating.• <u>Davis</u>: a thin line of glue should be applied sparingly over the wound edges.• <u>US 7,279,176</u>: 17. A method of reducing formation of surgical adhesions comprising administering to an individual in need thereof a biocompatible, polymerizable, macromer composition comprising at least one NO carrying region or an NO donor, wherein NO or the NO donor is complexed to the macromer composition, and wherein the NO or the NO donor is released from the macromer composition following polymerization in situ, under physiological conditions, wherein the macromer composition comprises regions selected from the group consisting of water soluble regions, tissue adhesive regions, and polymerizable end group regions.• <u>WO 97/22371</u>: In a general method for augmenting soft or hard tissue within the body of a mammalian subject, a first synthetic polymer containing two or more nucleophilic groups and a second synthetic polymer containing two or more electrophilic groups are administered simultaneously to a tissue site in need of augmentation and the reaction mixture is allowed to crosslink in situ to effect

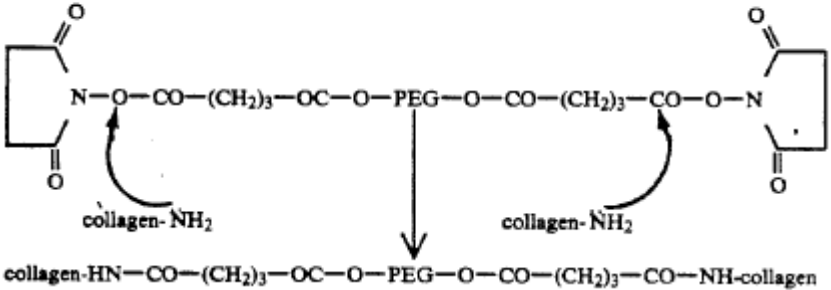
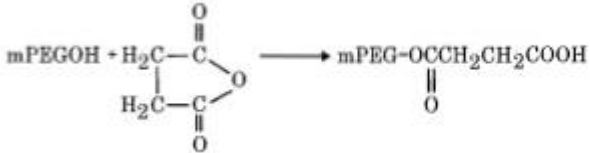
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>augmentation of the tissue.</p> <ul style="list-style-type: none">• <u>6,458,147</u>: The liquid material transforms as it is being dispersed as a result of cross-linking into an in situ-formed non-liquid covering structure. The covering structure intimately adheres and conforms to the surface the compromised tissue region, as FIG. 3 best shows.• <u>Otani</u>: In this study, a rapidly curable hydrogel glue was prepared as the seal for lung air leak. Mixing an aqueous solution of gelatin and poly(l-glutamic acid) with a water soluble carbodiimide produced a hydrogel. The mixed gelatin and PLGA aqueous solution sets in several seconds to a hydrogel at 37 °C with the addition of WSC; this is as short as conventional fibrin glue.
Components of the Composition		
Polymeric coating comprises water	[7,332,566, c1]: . A polymeric coating for a substrate comprising: water, a biocompatible visualization agent, and a biodegradable hydrogel	<ul style="list-style-type: none">• <u>Tse</u>: Cyanoacrylate chemistry relies on trace water (found in situ) to begin the polymerization process.• <u>Gayet & Fortier, J. Contr. Rel. 38 (1996) 177-184</u>: During the swelling process, water uptake by the hydrogel leads to the release of the drug in bulk solution.• <u>Prestwich et al.</u>: the hydrogels thus obtained were purified by repeated washings with water and were allowed to swell in water at 8 C. Gels swelled to approximately 10 times their original size.• <u>2014/0243428</u>: The disclosure provides for self-healing hydrogels, complex structures made therefrom, and use thereof, including use of the hydrogels as self-healing coatings, self-healing sealants, tissue adhesives, and drug carriers. Stability of Healed Hydrogels in Water and Effect of Temperature. <p>The completely healed hydrogels were immersed in deionized (DI) water for more than a month to determine their stability at ambient temperature. To determine the effect of temperature on the stability, the healed hydrogels were immersed in boiling water at 100° C. for 1 hour.</p> <ul style="list-style-type: none">• <u>4,839,345</u>: This invention relates to hydrated adhesive gels, especially hydrated adhesive gels for a self-adhesion cataplasm and pack agents having sheet shape• <u>5,328,955</u>: The collagen-polymer conjugates of the invention generally contain

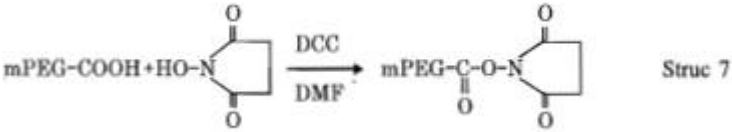
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>large amounts of water when formed.</p> <ul style="list-style-type: none">• <u>6,165,201</u>: Hydrogels inherently comprise water.• <u>Champagne</u>: Clinically proven, the toxic degradation products of longer-chain cyanoacrylates are barely detectable on extraction studies, such that they are widely considered non-toxic ... the adhesive was generally sprayed on using a spray gun nozzle and pressurized nitrogen gas, which left a thin, uniform layer of polymer on the tissue surface that dried into a flexible sheet.• <u>WO 2000/09087</u>: Preferably, the barrier does not undergo significant hydration.• <u>5,292,362</u>: The present invention is directed to a composition adapted to bond separated tissues together or to coat tissues or prosthetic materials to enhance strength and water tightness preferably upon the application of energy and particularly to a composition which is activated by a laser to form a strong, biologically compatible bond or coating.• <u>Zhao</u>: Hydrogels are generally considered as biocompatible materials because of their high water content. They have been used in a variety of biomaterial and biotechnology applications, such as tissue engineering, artificial organs, and drug delivery.• <u>Davis</u>: Teaches “medical version of super glue” comprises cyanoacrylates that are simultaneously nucleophile and electrophile. Requires water to initiate.• <u>6,162,241</u>: Water soluble hydrophilic oligomers available in the art may be incorporated into the biodegradable macromers.• <u>WO 97/22371</u>: Hydrophilic polymers and, in particular, various polyethylene glycols, are preferred for use in the compositions of the present invention. As used herein, the term "PEG" refers to polymers having the repeating structure (OCH₂CH₂)_n.
Mixing reactive precursor species comprising nucleophilic functional groups	<p>[7,009,034, c1]: mixing reactive precursor species comprising nucleophilic functional groups</p> <p>[7,009,034, c16]: wherein the polymer composition comprises electrophilic functional groups and nucleophilic functional groups that crosslink to each other.</p> <p>[7,332,566, c12]: mixing reactive precursor species comprising</p>	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: This invention relates generally to crosslinked polymer compositions comprising a first synthetic polymer containing multiple nucleophilic groups crosslinked using a second synthetic polymer containing multiple electrophilic groups, and to methods of using such compositions as bioadhesives, for tissue augmentation, in the prevention of surgical adhesions, and for coating surfaces of synthetic implants, as drug delivery matrices and for

Claim element	Patents in which element is found	Relevant Prior Art References
	nucleophilic functional groups, reactive precursor species comprising electrophilic functional groups [6,566,406, c6]: The method of claim 1, wherein providing a biocompatible small molecule crosslinker further comprises providing a biocompatible small molecule crosslinker having crosslinker functional groups that are nucleophilic. [8,535,705, c1]: mixing a first precursor with a second precursor in situ in the patient to form the hydro gel for treatment of the medical condition,	<p>ophthalmic applications.</p> <ul style="list-style-type: none">• <u>6,371,975</u>: As further defined in this Specification, a “chemically cross-linked” barrier material refers to all barrier materials not formed through the use of enzymes. Cross-linking can occur, e.g., as a result of energy (heat or light), or cross-linking chemical reactions (active esters, isocyanates, epoxides). Examples of these materials includes photo-cross-linked acrylates and nucleophilic attack of electrophiles.• <u>Gayet & Fortier</u>: [Col. 2 p. 178] “To a solution of BSA in 200 mM-pH 9.4 sodium borate buffer, the desired amount of activated PEG was added to achieve the correct OH/NH₂ molar ratio.”• Prestwich: Scheme 1. Nucleophile bound to Hyaluronic acid <div></div> <ul style="list-style-type: none">• US 5,583,114: The adhesive composition is readily formed from a two component mixture which includes a first part of a protein, preferably ... albumin ... and water-soluble crosslinking agent ...• US 6,051,648: The present invention discloses a crosslinked polymer composition comprising a first synthetic polymer containing two or more nucleophilic groups, and a second synthetic polymer containing two or more electrophilic groups which are capable of covalently bonding to one another to form a three dimensional matrix.• <u>WO 00/09087</u>: Nucleophilic functional group-containing macromers optionally may be mixed with electrophilic group-containing macromers to rapidly initiate polymerization.• <u>WO 2000/033764</u>: Structures A-E in FIG. 1 may be constructed, so long as the resulting functional polymer has the properties of low tissue toxicity, water solubility, and reactivity with nucleophilic functional groups. FIG. 2 illustrates various embodiments of nucleophilic biodegradable water-soluble crosslinkers and functional polymers suitable for use with electrophilic functional polymers and crosslinkers described herein.

Claim element	Patents in which element is found	Relevant Prior Art References
		<div><ul style="list-style-type: none">• <u>Tse</u>: Cyanoacrylate chemistry relies on trace water (found in situ) as the nucleophile to begin the polymerization process. Once the cyanoacrylate reacts with water, it becomes a nucleophilic agent.• US 5,614,587 (Rhee): Collagen given as nucleophile<div></div><ul style="list-style-type: none">• <u>Veronese</u>: Ribonuclease A and cupro-zinc superoxide dismutase (SOD) given as nucleophiles<div></div><div><div>$R =$ </div><div>$R =$ </div></div><ul style="list-style-type: none">• Ulbrich: Diamine PEG-derived nucleophiles disclosed</div>

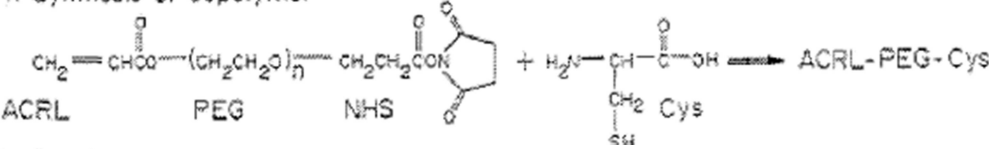
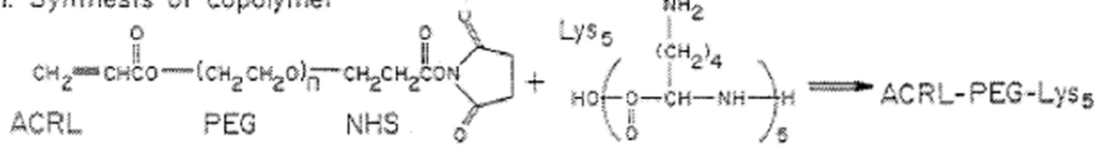
Claim element	Patents in which element is found	Relevant Prior Art References
		<div><p>$\text{H}_2\text{NCH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_x-\text{OCH}_2\text{CH}_2\text{NH}_2$</p><p>2</p><p>$\text{2} + \text{O}_2\text{N}-\text{C}_6\text{H}_4-\text{O}-\text{CO}-\underset{\text{C}_6\text{H}_5}{\underset{\text{CH}_2}{\text{CH}}}-\text{NH}-\text{CO}-(\text{CH}_2)_4-\text{CO}-\text{NH}-\underset{\text{C}_6\text{H}_5}{\underset{\text{CH}_2}{\text{CH}}}-\text{CO}-\text{O}-\text{C}_6\text{H}_4-\text{NO}_2 \longrightarrow$</p><p>15</p><p>$\left[\text{CH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_n-\text{OCH}_2\text{CH}_2\text{NH}-\underset{\text{C}_6\text{H}_5}{\underset{\text{CH}_2}{\text{CH}}}-\text{NH}-\text{CO}-(\text{CH}_2)_4-\text{CO}-\text{NH}-\underset{\text{C}_6\text{H}_5}{\underset{\text{CH}_2}{\text{CH}}}-\text{CO}-\text{NH} \right]_x$</p><p>17</p><ul style="list-style-type: none">4,839,345: The present invention is directed to a hydrated adhesive gel comprising a reaction product obtained by adding an aqueous solution of an N-hydroxyimidoester compound into an aqueous solution of gelatin which contains a protein having amino groups at the side groups thereof and a gelling retarder such as calcium chloride, urea, etc., and partially bridging the protein.<p>$\begin{array}{c} \begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_2-\text{C} \\ \parallel \\ \text{CH}_2-\text{C} \\ \parallel \\ \text{O} \end{array} \text{N}-\text{O}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{OCH}_2\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{O}-\text{N} \\ \begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_2-\text{C} \\ \parallel \\ \text{CH}_2-\text{C} \\ \parallel \\ \text{O} \end{array} \end{array} + \begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_2-\text{C} \\ \parallel \\ \text{CH}_2-\text{C} \\ \parallel \\ \text{O} \end{array} \text{N}-\text{O}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{OCH}_2\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{O}-\text{N}$</p><p>$\text{protein}-\text{NH}_2 + \text{H}_2\text{N}-\text{protein} \longrightarrow \text{protein}-\text{NH}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{OCH}_2\text{CH}_2-\text{O}-\text{CH}_2\text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{protein} +$</p></div>

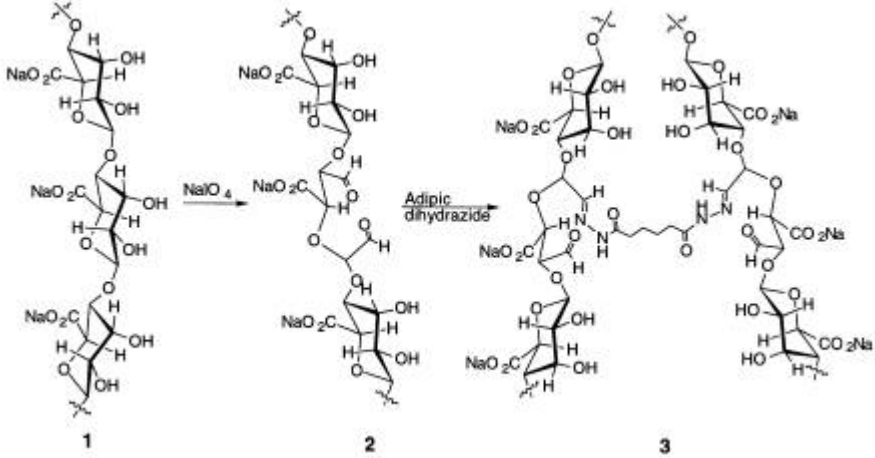
Claim element	Patents in which element is found	Relevant Prior Art References
		<ul style="list-style-type: none">5,328,955: collagen-amine nucleophiles: <div><p>FORMULA 1</p><p>S-PEG: Difunctional PEG Succinimidyl Glutarate</p><p>collagen-HN-CO-(CH₂)₃-OC-O-PEG-O-CO-(CH₂)₃-CO-NH-collagen</p></div>6,165,201: It should be understood, however, that hydrogels that crosslink by a variety of other mechanisms, for example, by interaction of electrophilic and nucleophilic functional groups, also may be advantageously used in accordance with the principles of the present invention.Berger & Pizzo, Blood: Coupling of SS-PEG-5 [i.e., succinimidyl succinate PEG] to rt-PA was carried out at 0.001 to 0.02 mol/L PEG concentrations and 100 ±g/mL rt-PA in 0.1 mol/L potassium phosphate, pH 8.0, containing 1 to 2 mol/L KSCN. Reactions were generally allowed to proceed for one hour at 0 °C.Champagne: teaches cyanoacrylates, which serve as both nucleophile and electrophile during polymerization the presence of ambient water.Dreborg: mPEGOH is suitable for modifying proteins ... Another frequently used method is to couple mPEGOH first to compounds which lead to the introduction of a carboxy group and which can then be activated for final reaction with the <div><p>Struc 4</p></div><p>protein: However, this derivative has an ester linkage which may be hydrolyzed in vivo ... For reaction with proteins, the mPEG acids have been activated in two different ways (e.g., synthesis of hydroxysuccinimide derivative):</p>

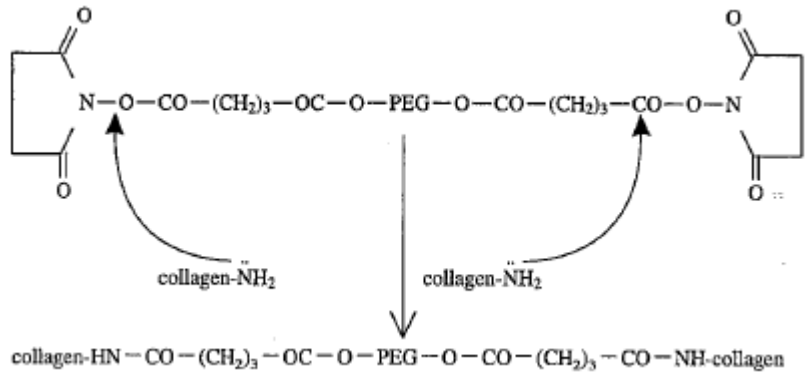
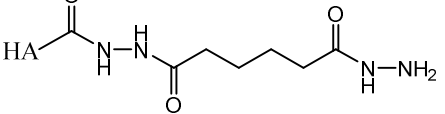
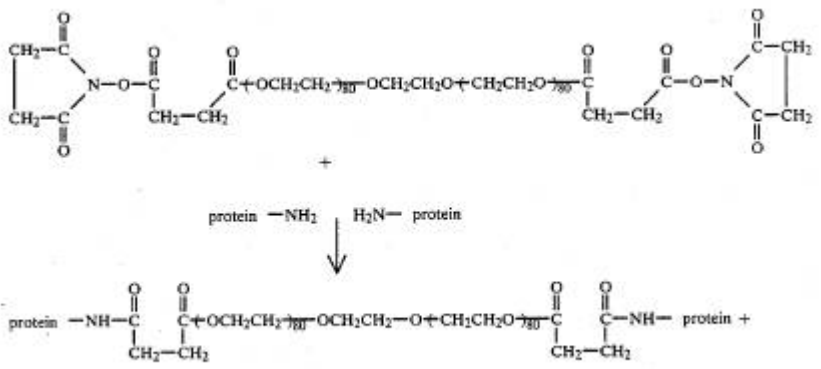
Claim element	Patents in which element is found	Relevant Prior Art References
		<div></div> <p>These activated mPEG acids react rapidly with the ε-amino lysine groups as well as with the terminal primary α-amino groups of the proteins. Coupling may also involve the phenolic group of tyrosine and mercapto groups.</p> <ul style="list-style-type: none">• <u>Ellis & Shaikh</u>: Fibrin glue, since the early 1970s, has gained popularity as a biologic adhesive amount the surgical specialties, and has been reported to be a safe bioadhesive and sealant ... We have been using histoacryl glue for closure of surgical incisions in facial and plastic reconstructive surgery ... the tissues to be approximated should be as dry as possible.• <u>Fortier et al.</u> <i>Biotechnol. Appl. Biochem.</i> 17 (1993) p.115-130: Five different poly(ethylene glycol)s (PEG) and three different monomethoxypoly(ethylene glycol)s (mPEG), of molecular masses ranging from 750 to 35000, were activated using 4-nitrophenyl chloroformate in acetonitrile in the presence of triethylamine for 5 h at 60°C. This was carried out in order to obtain a high yield of PEG-dinitrophenyl carbonates and mPEG-nitrophenyl carbonates respectively ... It was shown that the formation of the urethane bond between the o-NH2 group of lysine and the activated m/PEG occurred over a wide range of pH and temperature and at various molar ratios of reagents ... mPEGs (M_r values 750, 1900 and 5 000) and PEGs (M_r values 1450, 3 350, 10 000, 20 000 and 35 000) were derivatized using 4-nitrophenyl chloroformate in order to obtain a series of mPEG nitrophenyl carbonates and a series of PEG dinitrophenyl carbonates respectively ... The modification of HRP was carried out as follows. To 10 mg of HRP, dissolved in 5 ml of 0.1 M borate buffer solution at pH 9.4, was added a corresponding amount of one of the activated PEGs in order to obtain a final free NH2 groups of HRP /nitrophenyl carbonate groups molar ratio of 1: 4. The reaction mixture was kept at 4 °C overnight under gentle stirring (100 rev./min).• <u>Larwood & Szoka</u>: Polyethylene glycol diamine 6000 was coupled to methyl p-hydroxybenzimidate, and PEG 1900- and 5000 monomethyl ethers were coupled to tyramine and histamine.

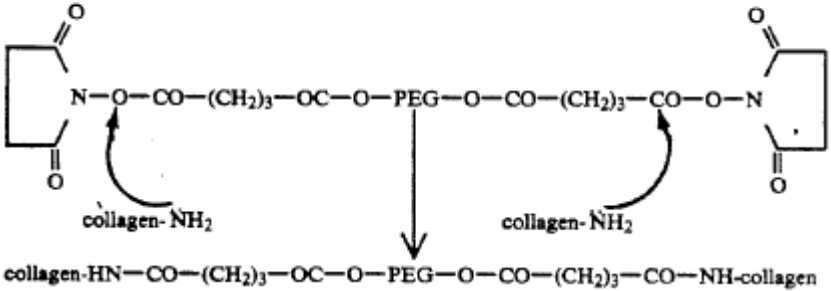
Claim element	Patents in which element is found	Relevant Prior Art References
		<p> $\text{MeO}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2\text{OH}$ (6) $\xrightarrow{\text{Nucleophile-Succinimide}}$ $\text{MeO}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{N}(\text{CH}_2\text{CH}_2)_2$ (7) $\xrightarrow{\text{Et}_3\text{N} / \text{H}_2\text{N}-\text{CH}_2\text{CH}_2-\text{R}}$ $\text{MeO}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{N}(\text{CH}_2\text{CH}_2)_2-\text{R}$ 8 R = 9 R = </p> <ul style="list-style-type: none"> WO 2000/09087: Polymerizable groups may be selected from nucleophilic groups and their salts that react further, for example with acylating agents. Useful nucleophilic groups may include amino or thiol groups ... Nucleophilic functional group-containing macromers optionally may be mixed with electrophilic group-containing macromers to rapidly initiate polymerization ... other useful groups include isocyanate, thiocyanate, and N-hydroxy succinimide esters such as succinimide. WO 2000/033764: Biocompatible crosslinked polymers, and methods for their preparation and use, are disclosed in which the biocompatible crosslinked polymers are formed from water soluble precursors having electrophilic and nucleophilic groups capable of reacting and crosslinking in situ. Methods for making the resulting biocompatible crosslinked polymers biodegradable or not are provided, as are methods for controlling the rate of degradation. The crosslinking reactions may be carried out in situ on organs or tissues or outside the body. Applications for such biocompatible crosslinked polymers and their precursors

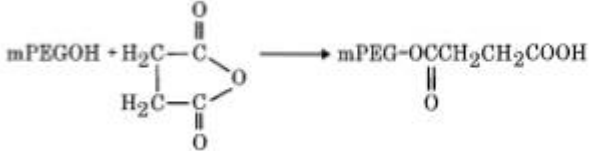
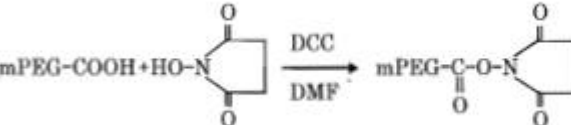
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>include controlled delivery of drugs, prevention of post-operative adhesions, coating of medical devices such as vascular grafts, wound dressings and surgical sealants.</p> <ul style="list-style-type: none">• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddlesFifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8.

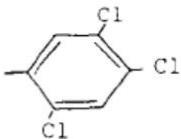

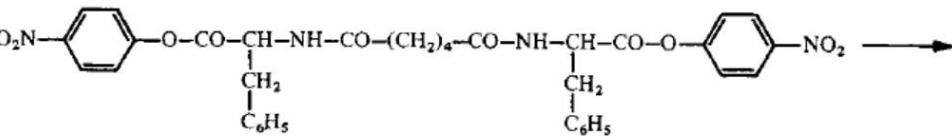
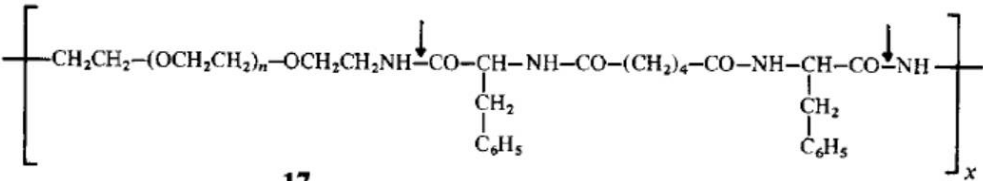
Claim element	Patents in which element is found	Relevant Prior Art References
		<div>1. Synthesis of copolymer</div> <div></div> <div>1. Synthesis of copolymer</div> <div></div> <ul style="list-style-type: none">6,162,241: The monomers or macromers preferably include crosslinkable groups which are capable of forming covalent bonds while in aqueous solution. These crosslinkable groups permit crosslinking of the macromers to form a gel. Other crosslinking chemistries which may be used include, for example, reaction of amines or alcohols with isocyanate or isothiocyanate, or of amines or thiols with aldehydes, epoxides, oxiranes, or cyclic imines.WO 97/22371: Synthetic polymers containing multiple nucleophilic groups are also referred to generically herein as "multi-nucleophilic polymers". For use in the present invention, multi-nucleophilic polymers must contain at least two, more preferably, at least three, nucleophilic groups. If a synthetic polymer containing only two nucleophilic groups is used, a synthetic polymer containing three or more electrophilic groups must be used in order to obtain a three-dimensional crosslinked network ... Preferred multi-nucleophilic polymers include: (i) synthetic polypeptides that have been synthesized to contain two or more primary amino groups or thiol groups; and (ii) polyethylene glycols that have been modified to contain two or more primary amino groups or thiol groups.6,458,147: In a preferred embodiment, the material of the covering structure is a protein/polymer composite hydrogel. The material is most preferably formed from the mixture of a protein solution and a solution of an electrophilic derivative of a hydrophilic polymer with a functionality of at least three. The material is nontoxic, biodegradable, and possesses mechanical properties such as cohesive strength, adhesive strength, and elasticity sufficient to block or arrest diffuse

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>organ bleeding, or to block or arrest seepage as a result of anastomosis, or to seal lung punctures. The cross-linking group is responsible for the cross-linking of the albumin, as well as the binding to the tissue substrate. The cross-linking group can be selected to selectively react with sulfhydryl groups, selectively react with amines, or can be selected to react with sulfhydryl, primary amino, and secondary amino groups</p> <ul style="list-style-type: none"><u>Bouhadir et al:</u> <u>Otani:</u> In this study, a rapidly curable hydrogel glue was prepared as the seal for lung air leak. Mixing an aqueous solution of gelatin and poly(l-glutamic acid) with a water soluble carbodiimide produced a hydrogel. The mixed gelatin and PLGA aqueous solution sets in several seconds to a hydrogel at 37 °C with the addition of WSC; this is as short as conventional fibrin glue.<u>US 6,051,648 (Rhee):</u> A preferred composition of the invention comprises polyethylene glycol containing two or more primary amino groups as the first synthetic polymer, and polyethylene glycol containing two or more succinimidyl groups (a five-membered ring structure represented herein as --N(COCH2)2) as the second synthetic polymer.<u>US 5,614,587 (Rhee):</u> Collagen given as nucleophile
Nucleophilic functional group is an amine	<p>[6,566,406, c7]: The method of claim 6, wherein providing a biocompatible small molecule crosslinker having crosslinker functional groups that are nucleophilic further comprises providing a biocompatible small molecule crosslinker wherein the crosslinker functional groups are amines.</p> <p>[8,003,705, c1]: A method for making a medical device, the method comprising:</p>	

Claim element	Patents in which element is found	Relevant Prior Art References
	<p>providing at least a first biocompatible precursor having least two electrophilic functional groups, and providing at least a second biocompatible precursor comprising at least two primary amine functional groups;</p> <p>[8,003,705, c11]: providing a first biocompatible precursor having at least two electrophilic functional groups, a second biocompatible precursor comprising at least two primary amine functional groups, a third biocompatible precursor comprising at least two primary amine functional groups;</p>	<div></div> <ul style="list-style-type: none">• <u>Gayet & Fortier</u>: To a solution of BSA (50 mg/mL) in 200 mM-pH 9.4 sodium borate buffer, the desired amount of activated PEG was added to achieve the correct OH/NH₂ molar ratio.• <u>Prestwich</u>: Scheme 1. Nucleophile bound to Hyaluronic acid is amine (hydrazide):<div></div>• <u>4,839,345</u>: shows amino groups bound to proteins as nucleophiles:<div></div>

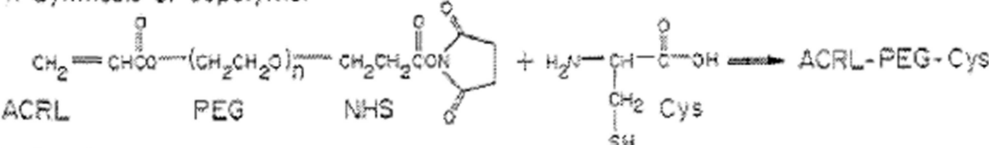
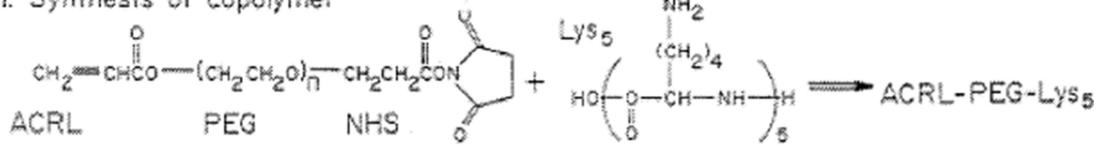
Claim element	Patents in which element is found	Relevant Prior Art References
		<ul style="list-style-type: none">5,328,955: collagen-amine nucleophiles: <div><p>FORMULA 1</p><p>S-PEG: Difunctional PEG Succinimidyl Glutarate</p><p>collagen-HN-CO-(CH₂)₃-OC-O-PEG-O-CO-(CH₂)₃-CO-NH-collagen</p></div>6,165,201: Preferred hydrogel systems are those biocompatible multi-component systems that spontaneously crosslink when the components are mixed, but wherein the two or more components are individually stable for the duration of the deposition process. Such systems include, for example, contain macromers that are di or multifunctional amines in one component and di or multifunctional oxirane containing moieties in the other component.Berger & Pizzo, Blood: Coupling of SS-PEG-5 [i.e., succinimidyl succinate PEG] to rt-PA was carried out at 0.001 to 0.02 mol/L PEG concentrations and 100 ±g/mL rt-PA in 0.1 mol/L potassium phosphate, pH 8.0, containing 1 to 2 mol/L KSCN. Reactions were generally allowed to proceed for one hour at 0 °C.Berger & Pizzo, Blood: Coupling of SS-PEG-5 [i.e., succinimidyl succinate PEG] to rt-PA was carried out at 0.001 to 0.02 mol/L PEG concentrations and 100 ±g/mL rt-PA in 0.1 mol/L potassium phosphate, pH 8.0, containing 1 to 2 mol/L KSCN. Reactions were generally allowed to proceed for one hour at 0 °C ... the degree of modification of lysine residues was determined by titration with TNBS in 0.02 mol/L sodium borate buffer, pH 8.5, containing 2 mol/L KSCN...Dreborg: mPEGOH is suitable for modifying proteins ... Another frequently used method is to couple mPEGOH first to compounds which lead to the introduction of a carboxy group and which can then be activated for final reaction with the

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		<div style="text-align: right;">Struc 4</div>  <p>protein:</p> <p>However, this derivative has an ester linkage which may be hydrolyzed in vivo ...</p> <p>For reaction with proteins, the mPEG acids have been activated in two different ways (e.g., synthesis of hydroxysuccinimide derivative):</p> <div style="text-align: right;">Struc 7</div>  <p>These activated mPEG acids react rapidly with the ε-amino lysine groups as well as with the terminal primary α-amino groups of the proteins. Coupling may also involve the phenolic group of tyrosine and mercapto groups.</p> <ul style="list-style-type: none"> • <u>Larwood & Szoka</u>: Polyethylene glycol diamine 6000 was coupled to methyl p-hydroxybenzimidate, and PEG 1900- and 5000 monomethyl ethers were coupled to tyramine and histamine.

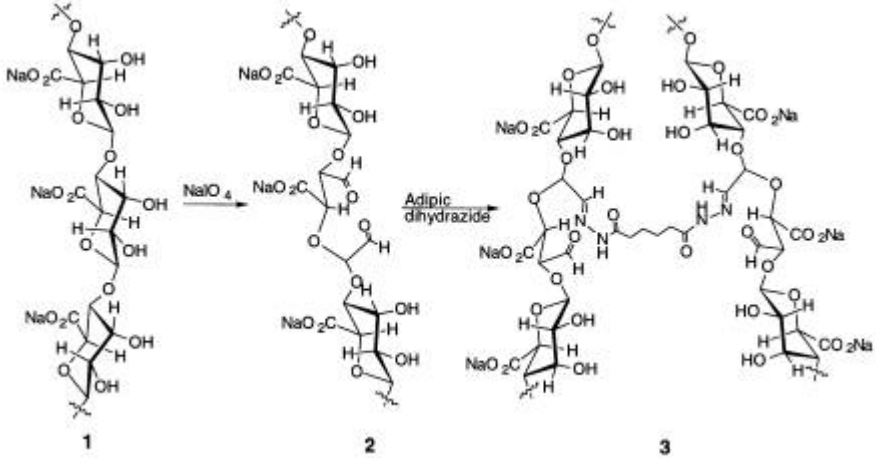
Claim element	Patents in which element is found	Relevant Prior Art References
		<div>$\text{CH}_3\text{O}-(\text{C}_2\text{H}_4\text{O})_n-\text{H} + \text{Cl}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{R} \longrightarrow \text{CH}_3\text{O}-(\text{C}_2\text{H}_4\text{O})_n-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{R} + \text{H}_2\text{N}-\text{Protein}$<div>$\downarrow$$\text{CH}_3\text{O}-(\text{C}_2\text{H}_4\text{O})_n-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}-\text{Protein}$</div></div> <div><div>$\text{R} =$</div><div>$\text{R} =$</div></div> <div><ul style="list-style-type: none">Ulbrich: Diamine PEG-derived nucleophiles disclosed<div>$\text{H}_2\text{NCH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_x-\text{OCH}_2\text{CH}_2\text{NH}_2$<div>2</div></div><div><div>$\text{2} +$</div><div>15</div></div><div><div></div><div>17</div></div><div><ul style="list-style-type: none">US 2006/0062768: The Nucleophilic Component In the illustrated embodiment, the nucleophilic component 14 includes a human or animal protein derived from</div></div>

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>an autologous source. By “autologous source,” it is meant that the human or animal protein is derived from the individual human or animal that is to be treated using the solid matrix composition 16. As will be demonstrated later, the autologous source can include presence of an anticoagulant (e.g., heparin) to facilitate handling.</p> <p>The autologous protein can be a local region of tissue of the human or animal that is to be treated. Alternatively, or in combination, the autologous protein can be whole blood drawn from the human or animal to be treated, or a blood component or blood derivative that is harvested from blood drawn from the human or animal to be treated. The blood can be drawn at the time that the composition 16 is mixed. Alternatively, the blood can be drawn, processed, and stored beforehand in anticipation of its use in forming the composition 16 during or following later-scheduled surgery or therapeutic procedure (e.g., cosmetic surgery, stem cell delivery, lung resection, etc.). For example, the blood-derived protein can comprise albumin, or bone marrow stromal stem cells (SSC), or platelet gel (PG), which may be obtained by platelet-rich plasma (PRP) harvested from whole blood. PRP also carries intrinsic growth factors, such as PDGF, TGFb, and FGF. The use of blood or blood compounds derived from autologous blood can itself thus provide intrinsic growth benefits, e.g., the promotion of soft tissue revascularization, and/or acceleration of bone graft healing not otherwise achieved when using pooled, random donor blood products. Use of a natural, autologous blood or blood compound as the nucleophilic component 14 obviates the use of pooled blood products derived from random human or animal donors. The use of an autologous blood or blood compounds makes possible great compatibility within patients. Such a system could be adapted for human or animal purposes; i.e., human blood would be used for treatment of a human and animal blood would be used when treating an animal.</p> <p>As another example, the additive component 18 can increase the number of nucleophilic sites to cross-link with the electrophilic component 12. The additive component 18 may include additional human or animal protein, e.g., a human serum albumin (HSA) for human indications, or an animal serum albumin in the case of animal indications. For human applications, the additive component 18</p>

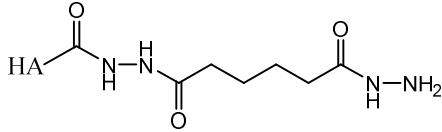
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>preferably contains less than 20% HSA. The additive component 18 may also include an amine compound, e.g., a poly(ethylene glycol)-amine (PEG-NH2) compound or lycine.</p> <ul style="list-style-type: none">• <u>WO 2000/09087</u>: Polymerizable groups may be selected from nucleophilic groups and their salts that react further, for example with acylating agents. Useful nucleophilic groups may include amino or thiol groups ... Nucleophilic functional group-containing macromers optionally may be mixed with electrophilic group-containing macromers to rapidly initiate polymerization ... other useful groups include isocyanate, thiocyanate, and N-hydroxy succinimide esters such as succinimide.• <u>WO 2000/033764</u>: Preferably, each precursor comprises only nucleophilic or only electrophilic functional groups, so long as both nucleophilic and electrophilic precursors are used in the crosslinking reaction. Thus, for example, if a crosslinker has nucleophilic functional groups such as amines, the functional polymer may have electrophilic functional groups such as N-hydroxysuccinimides .• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddlesFifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8.

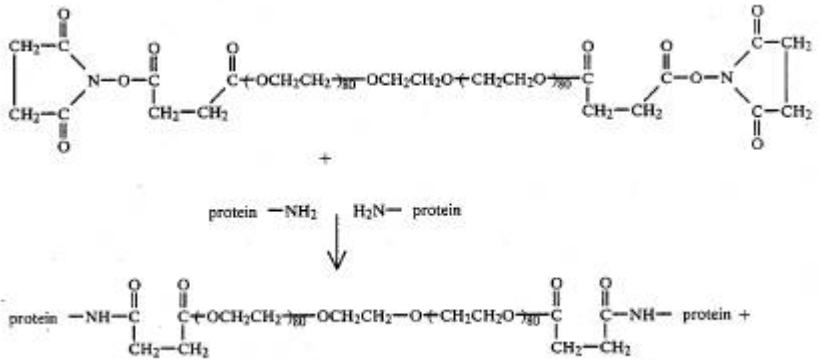
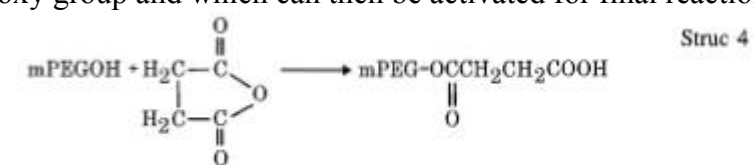
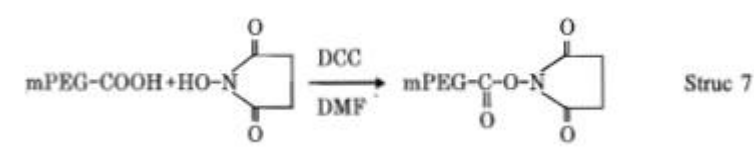
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>$\text{PEG}-\text{COO}-\text{R}-\text{COO}-\text{NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG}-\text{COO}-\text{R}-\text{CONH-protein}$</p> <p><i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.</p> <ul style="list-style-type: none">7,279,176: 1. Synthesis of copolymer  1. Synthesis of copolymer 6,162,241: The monomers or macromers preferably include crosslinkable groups which are capable of forming covalent bonds while in aqueous solution. These crosslinkable groups permit crosslinking of the macromers to form a gel. Other crosslinking chemistries which may be used include, for example, reaction of amines or alcohols with isocyanate or isothiocyanate, or of amines or thiols with aldehydes, epoxides, oxiranes, or cyclic imines.WO 97/22371: Synthetic polymers containing multiple nucleophilic groups are also referred to generically herein as "multi-nucleophilic polymers". For use in the present invention, multi-nucleophilic polymers must contain at least two, more preferably, at least three, nucleophilic groups. If a synthetic polymer containing only two nucleophilic groups is used, a synthetic polymer containing three or more electrophilic groups must be used in order to obtain a three-dimensional crosslinked network ... Preferred multi-nucleophilic polymers include: (i)

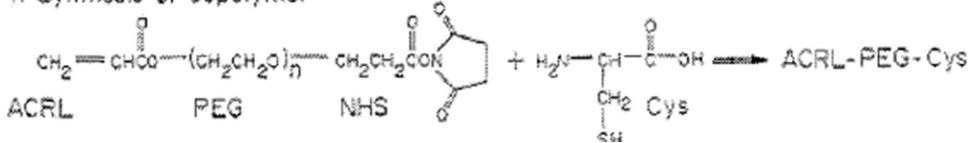
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>synthetic polypeptides that have been synthesized to contain two or more primary amino groups or thiol groups; and (ii) polyethylene glycols that have been modified to contain two or more primary amino groups or thiol groups.</p> <ul style="list-style-type: none">• <u>6,371,975</u>: As further defined in this Specification, a “chemically cross-linked” barrier material refers to all barrier materials not formed through the use of enzymes. Cross-linking can occur, e.g., as a result of energy (heat or light), or cross-linking chemical reactions (active esters, isocyanates, epoxides). Examples of these materials includes photo-cross-linked acrylates and nucleophilic attack of electrophiles. The cross-linking group is responsible for the cross-linking of the albumin, as well as the binding to the tissue substrate. The cross-linking group can be selected to selectively react with sulfhydryl groups, selectively react with amines, or can be selected to react with sulfhydryl, primary amino, and secondary amino groups.• <u>6,458,147</u>: In a preferred embodiment, the material of the covering structure is a protein/polymer composite hydrogel. The material is most preferably formed from the mixture of a protein solution and a solution of an electrophilic derivative of a hydrophilic polymer with a functionality of at least three. The material is nontoxic, biodegradable, and possesses mechanical properties such as cohesive strength, adhesive strength, and elasticity sufficient to block or arrest diffuse organ bleeding, or to block or arrest seepage as a result of anastomosis, or to seal lung punctures. The cross-linking group is responsible for the cross-linking of the albumin, as well as the binding to the tissue substrate. The cross-linking group can be selected to selectively react with sulfhydryl groups, selectively react with amines, or can be selected to react with sulfhydryl, primary amino, and secondary amino groups• <u>Bouhadir et al</u>:

Claim element	Patents in which element is found	Relevant Prior Art References
		
Nucleophile is dilysine, trilysine or tetralysine	<p>[7,332,566, c2]: The polymeric coating of claim 1 wherein the hydrogel comprises a reaction product of a synthetic polymer that comprises electrophilic functional groups and at least one of dilysine, trilysine or tetralysine.</p> <p>[7,332,566, c13]</p> <p>[6,566,406, c26]</p>	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: Preferred multi-nucleophilic polypeptides are synthetic polypeptides that have been synthesized to incorporate amino acids containing primary amino groups (such as lysine) and/or amino acids containing thiol groups (such as cysteine). Poly(lysine), a synthetically produced polymer of the amino acid lysine (145 MW), is particularly preferred. Poly(lysine)s have been prepared having anywhere from 6 to about 4,000 primary amino groups, corresponding to molecular weights of about 870 to about 580,000.• <u>Berger & Pizzo, Blood</u>: Coupling of SS-PEG-5 [<i>i.e.</i>, <i>succinimidyl succinate PEG</i>] to rt-PA was carried out at 0.001 to 0.02 mol/L PEG concentrations and 100 ±g/mL rt-PA in 0.1 mol/L potassium phosphate, pH 8.0, containing 1 to 2 mol/L KSCN. Reactions were generally allowed to proceed for one hour at 0 °C ... the degree of modification of lysine residues was determined by titration with TNBS in 0.02 mol/L sodium borate buffer, pH 8.5, containing 2 mol/L KSCN...• <u>Fortier et al. Biotechnol. Appl. Biochem.</u> 17 (1993) p.115-130: Five different poly(ethylene glycol)s (PEG) and three different monomethoxypoly(ethylene glycol)s (mPEG), of molecular masses ranging from 750 to 35000, were activated using 4-nitrophenyl chloroformate in acetonitrile in the presence of triethylamine for 5 h at 60°C. This was carried out in order to obtain a high yield of

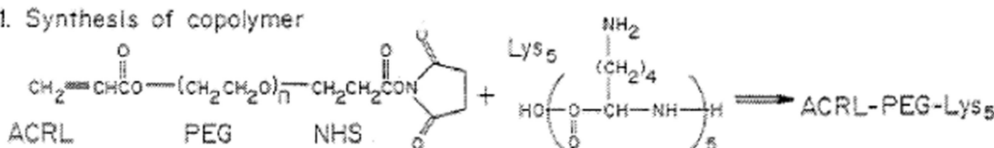
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>PEG-dinitrophenyl carbonates and mPEG-nitrophenyl carbonates respectively ... It was shown that the formation of the urethane bond between the o-NH2 group of lysine and the activated m/PEG occurred over a wide range of pH and temperature and at various molar ratios of reagents ... mPEGs (M_r values 750, 1900 and 5 000) and PEGs (M_r values 1450, 3 350, 10 000, 20 000 and 35 000) were derivatized using 4-nitrophenyl chloroformate in order to obtain a series of mPEG nitrophenyl carbonates and a series of PEG dinitrophenyl carbonates respectively ... The modification of HRP was carried out as follows. To 10 mg of HRP, dissolved in 5 ml of 0.1 M borate buffer solution at pH 9.4, was added a corresponding amount of one of the activated PEGs in order to obtain a final free NH2 groups of HRP /nitrophenyl carbonate groups molar ratio of 1: 4. The reaction mixture was kept at 4 °C overnight under gentle stirring (100 rev./min).</p> <ul style="list-style-type: none">• <u>WO 2000/033764</u>: When Structures Q-T in FIG. 4 are functional polymers they may be multifunctional graft or branch type water-soluble copolymers with terminal amine groups. Structures P-T in FIG. 4 need not have polymeric cores and may be small molecule crosslinkers. In that case, the core may comprise a small molecule like ethoxylated glycerol, inositol, trimethylolpropane, dilysine etc. to form the resultant crosslinker.• <u>7,279,176</u>: <p>1. Synthesis of copolymer</p><p>1. Synthesis of copolymer</p><p>• <u>WO 97/22371</u>: Synthetic polymers containing multiple nucleophilic groups are also referred to generically herein as "multi-nucleophilic polymers". For use in the present invention, multi-nucleophilic polymers must contain at least two, more preferably, at least three, nucleophilic groups. If a synthetic polymer containing</p>

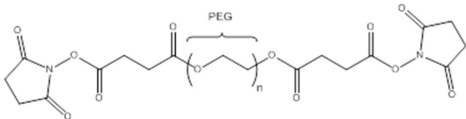
Claim element	Patents in which element is found	Relevant Prior Art References
		only two nucleophilic groups is used, a synthetic polymer containing three or more electrophilic groups must be used in order to obtain a three-dimensional crosslinked network ... Preferred multi-nucleophilic polymers include: (i) synthetic polypeptides that have been synthesized to contain two or more primary amino groups or thiol groups; and (ii) polyethylene glycols that have been modified to contain two or more primary amino groups or thiol groups. Preferred multi-nucleophilic polypeptides are synthetic polypeptides that have been synthesized to incorporate amino acids containing primary amino groups (such as lysine) and/or amino acids containing thiol groups (such as cysteine).
Nucleophiles comprise primary amines or thiols	<p>[7,332,566, c14]: The method of claim 12 wherein the nucleophilic functional groups comprise primary amines or primary thiols.</p> <p>[7,332,566, c36]: The method of claim 25 wherein the hydrogel comprises a reaction product of a synthetic polymer that comprises electrophilic functional groups and a synthetic polymer that comprises a plurality of primary amines or primary thiols, wherein the reaction product is formed through the crosslinking between the electrophilic the functional groups of the synthetic polymer and the plurality of primary amines or primary thiols in the other synthetic polymer.</p> <p>[7,592,418, c3]: The method of claim 1 wherein the hydrogel comprises a reaction product of a synthetic polymer that comprises electrophilic functional groups and a synthetic polymer that comprises a plurality of primary amines or primary thiols, wherein the reaction product is formed through the crosslinking between the electrophilic functional groups of the synthetic polymer and the plurality of primary amines or primary thiols in the other synthetic polymer.</p> <p>[7,592,418, c22]: The method of claim 3 wherein the synthetic polymer comprises the plurality of primary amines.</p> <p>[6,566,406, c18]: The method of claim 17 wherein the first</p>	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: Preferred multi-nucleophilic polypeptides are synthetic polypeptides that have been synthesized to incorporate amino acids containing primary amino groups (such as lysine) and/or amino acids containing thiol groups (such as cysteine). Poly(lysine), a synthetically produced polymer of the amino acid lysine (145 MW), is particularly preferred. Poly(lysine)s have been prepared having anywhere from 6 to about 4,000 primary amino groups, corresponding to molecular weights of about 870 to about 580,000.• <u>Prestwich</u>: Scheme 1. Nucleophile bound to Hyaluronic acid is amine (hydrazide): • <u>4,839,345</u>: shows amino groups bound to proteins as nucleophiles:

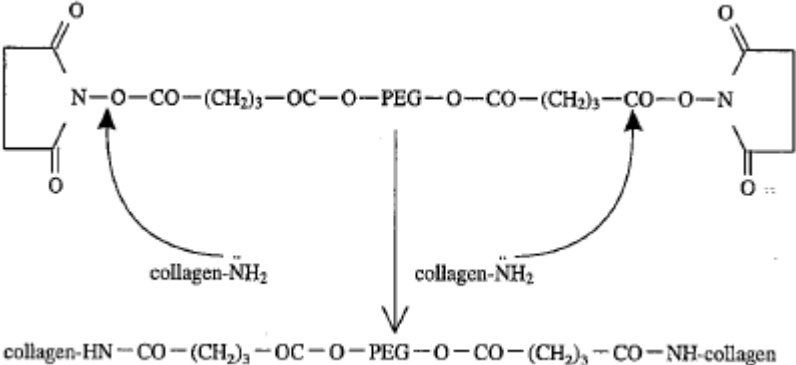
Claim element	Patents in which element is found	Relevant Prior Art References
	<p>functional groups are the nucleophiles and are amines and the second functional groups are the electrophiles and are succinimides. [8,535,705, c1]; and the second biocompatible synthetic hydrophilic polymer precursor comprising at least two nucleophilic amine functional groups; and</p>	<div></div> <ul style="list-style-type: none">6,165,201: Alternatively, the two or more solutions may include macromers that contain groups that demonstrate activity towards other functional groups such as amines, imines, thiolsDreborg: mPEGOH is suitable for modifying proteins ... Another frequently used method is to couple mPEGOH first to compounds which lead to the introduction of a carboxy group and which can then be activated for final reaction with the <div></div> <p>protein: However, this derivative has an ester linkage which may be hydrolyzed in vivo ... For reaction with proteins, the mPEG acids have been activated in two different ways (e.g., synthesis of hydroxysuccinimide derivative):</p> <div></div> <p>These activated mPEG acids react rapidly with the ε-amino lysine groups as well as with the terminal primary α-amino groups of the proteins. Coupling may also involve the phenolic group of tyrosine and mercapto groups.</p>

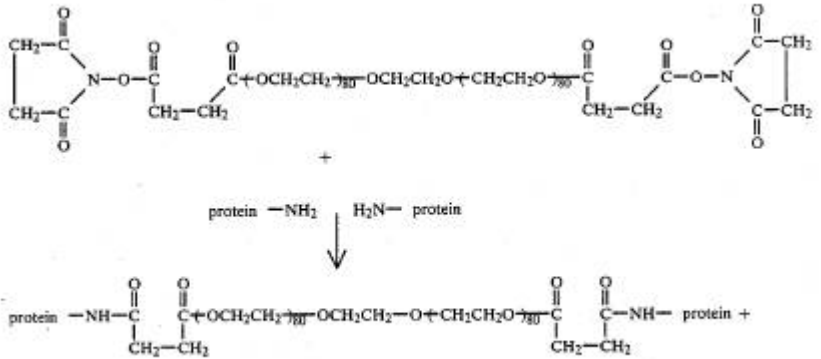
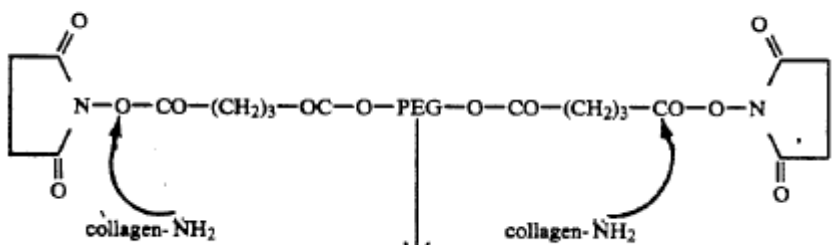
Claim element	Patents in which element is found	Relevant Prior Art References
		<ul style="list-style-type: none">• <u>WO 2000/09087</u>: Polymerizable groups may be selected from nucleophilic groups and their salts that react further, for example with acylating agents. Useful nucleophilic groups may include amino or thiol groups ... Nucleophilic functional group-containing macromers optionally may be mixed with electrophilic group-containing macromers to rapidly initiate polymerization ... other useful groups include isocyanate, thiocyanate, and N-hydroxy succinimide esters such as succinimide.• <u>WO 2000/ 033764</u>: Structures G, H, I and J in FIG. 2 may represent multifunctional branched or graft type copolymers having water-soluble core extended with oligohydroxy acid polymer and terminated with amine or thiol groups.• <u>7,279,176</u>: 1. Synthesis of copolymer • <u>6,162,241</u>: The monomers or macromers preferably include crosslinkable groups which are capable of forming covalent bonds while in aqueous solution. These crosslinkable groups permit crosslinking of the macromers to form a gel. Other crosslinking chemistries which may be used include, for example, reaction of amines or alcohols with isocyanate or isothiocyanate, or of amines or thiols with aldehydes, epoxides, oxiranes, or cyclic imines.• <u>WO 97/22371</u>: Synthetic polymers containing multiple nucleophilic groups are also referred to generically herein as "multi-nucleophilic polymers". For use in the present invention, multi-nucleophilic polymers must contain at least two, more preferably, at least three, nucleophilic groups. If a synthetic polymer containing only two nucleophilic groups is used, a synthetic polymer containing three or more electrophilic groups must be used in order to obtain a three-dimensional crosslinked network ... Preferred multi-nucleophilic polymers include: (i) synthetic polypeptides that have been synthesized to contain two or more primary amino groups or thiol groups; and (ii) polyethylene glycols that have been

Claim element	Patents in which element is found	Relevant Prior Art References
		modified to contain two or more primary amino groups or thiol groups.
Free of amino acid sequences of more than about four residues in number	[7,332,566, c9]: The polymeric coating of claim 1 wherein the hydrogel is free of amino acid sequences of more than about four residues in number. [7,332,566, c21] [7,332,566, c31] [7,592,418, c7]	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: Polyethylene glycol can be chemically modified to contain multiple primary amino or thiol groups• <u>Prestwich</u>: Scheme 1. Nucleophile bound to Hyaluronic acid is amine (hydrazide): No amino acids <div></div> <ul style="list-style-type: none">• <u>Ellis & Shaikh</u>: Fibrin glue, since the early 1970s, has gained popularity as a biologic adhesive amount the surgical specialties, and has been reported to be a safe bioadhesive and sealant ... We have been using histoacryl glue for closure of surgical incisions in facial and plastic reconstructive surgery ... the tissues to be approximated should be as dry as possible. Cyanoacrylates do not have >4 amines.• <u>Sawhney et al., Macromolecules, (1993) 26, 581-587</u>: Macromers having a poly(ethylene glycol) central block, extended with oligomers of a-hydroxy acids such as oligo(dl-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation of cross-linked gels. These gels degrade upon hydrolysis of the oligo(a-hydroxy acid) regions into poly(ethylene glycol), the a-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular drug delivery.• <u>WO 2000/033764</u>: When Structures Q-T in FIG. 4 are functional polymers they may be multifunctional graft or branch type water-soluble copolymers with terminal amine groups. Structures P-T in FIG. 4 need not have polymeric cores and may be small molecule crosslinkers. In that

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>case, the core may comprise a small molecule like ethoxylated glycerol, inositol, trimethylolpropane, dilysine etc. to form the resultant crosslinker.</p> <ul style="list-style-type: none">• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddlesFifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8. <p>$\text{PEG-COO-R-COO-NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG-COO-R-CONH-protein}$</p> <p><i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.</p> <ul style="list-style-type: none">• <u>7,279,176</u>: 1. Synthesis of copolymer • <u>WO 97/22371</u>: Synthetic polymers containing multiple nucleophilic groups are also referred to generically herein as "multi-nucleophilic polymers". For use in the present invention, multi-nucleophilic polymers must contain at least two, more preferably, at least three, nucleophilic groups. If a synthetic polymer containing only two nucleophilic groups is used, a synthetic polymer containing three or more electrophilic groups must be used in order to obtain a

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		three-dimensional crosslinked network ... Preferred multi-nucleophilic polymers include: (i) synthetic polypeptides that have been synthesized to contain two or more primary amino groups or thiol groups; and (ii) polyethylene glycols that have been modified to contain two or more primary amino groups or thiol groups.
Reactive precursor species comprising electrophilic functional groups,	<p>[7,009,034, c1]: reactive precursor species comprising electrophilic functional groups</p> <p>[8,003,705, c1]: A method for making a medical device, the method comprising:</p> <p>providing at least a first biocompatible precursor having least two electrophilic functional groups, and providing at least a second biocompatible precursor comprising at least two primary amine functional groups;</p> <p>[8,535,705, c1]: with the first biocompatible synthetic hydrophilic polymer precursor having a water solubility of at least 1 gram per 100 milliliters and comprising at least two electrophilic functional groups;</p>	<ul style="list-style-type: none">• <u>Gayet & Fortier</u>: [Col. 1-2, p. 178] “Activation of PEG with p-nitrophenylchloroformate was carried out as previously described and yielded di(p-nitro-phenylcarbonate)-PEG”• <u>Prestwich</u>: See Scheme 2: N-hydroxysuccinimide esters are noted as electrophilic in ‘034.• <u>US 5,583,114</u>: The adhesive composition is readily formed from a two component mixture which includes a first part of a protein, preferably ... albumin ... and water-soluble crosslinking agent ... <p>PEG-SS2:</p> <div></div> <ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: The present invention discloses a crosslinked polymer composition comprising a first synthetic polymer containing two or more nucleophilic groups, and a second synthetic polymer containing two or more electrophilic groups which are capable of covalently bonding to one another to form a three dimensional matrix.• <u>WO 00/09087</u>: Random copolymers of monomers that form water soluble polymers also may be used, for example, copolymers of vinyl amine and allyl alcohol. These types of random copolymers are preferred when the crosslinking reaction is mediated by nucleophilic or electrophilic functional groups.

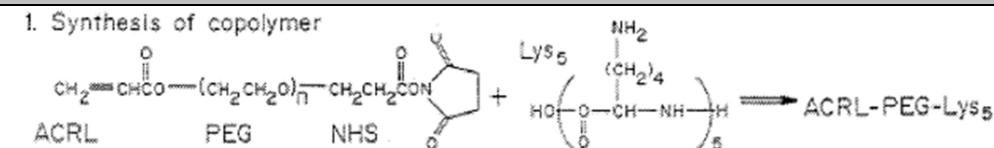
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>Electrophilic groups that may be useful to react with the aforementioned nucleophilic groups may include carboxyl groups that may or may not be separated from the polymeric main chain (either at the chain ends or along the backbone) by spacer groups that may contain ester linkages (for example esters of succinic acid, carboxymethyl esters, esters of propionic, adipic, or amino acids), among others.</p> <ul style="list-style-type: none">• <u>WO 2000/033764</u>: FIGS. 1 to 5 illustrate various embodiments of preferred crosslinkers and functional polymers. FIG. 1 illustrates possible configurations of degradable electrophilic crosslinkers or functional polymers. <p>The novel biocompatible crosslinked polymers of this invention are formed from the reaction of precursors having electrophilic and nucleophilic functional groups.</p> <ul style="list-style-type: none">• <u>Tse</u>: Cyanoacrylate chemistry relies on trace water (found in situ) to begin the polymerization process. They cyanoacrylate begins as an electrophile that turns to a nucleophile.• <u>US 5,614,587 (Rhee)</u>: Collagen given as nucleophile <div></div> <ul style="list-style-type: none">• <u>4,839,345</u>: NHS esters as electrophilic leaving groups

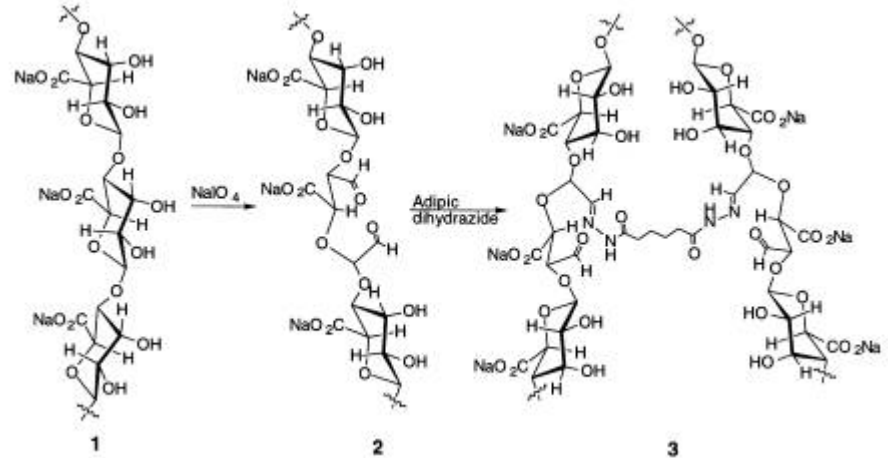
Claim element	Patents in which element is found	Relevant Prior Art References
		<div></div> <ul style="list-style-type: none">5,328,955: NHS-groups as electrophilic portion: <div><p>FORMULA 1</p><p>S-PEG: Difunctional PEG Succinimidyl Glutarate</p><p>collagen-NH₂</p><p>collagen-NH₂</p><p>collagen-HN-CO-(CH₂)₃-OC-O-PEG-O-CO-(CH₂)₃-CO-NH-collagen</p></div>6,165,201: Preferred hydrogel systems are those biocompatible multi-component systems that spontaneously crosslink when the components are mixed, but wherein the two or more components are individually stable for the duration of the deposition process. Such systems include, for example, contain macromers that are di or multifunctional amines in one component and di or multifunctional oxirane containing moieties in the other component.Berger & Pizzo, Blood: Coupling of SS-PEG-5 [i.e., succinimidyl succinate PEG] to rt-PA was carried out at 0.001 to 0.02 mol/L PEG concentrations and 100 ±g/mL rt-PA in 0.1 mol/L potassium phosphate, pH 8.0, containing 1 to 2 mol/L

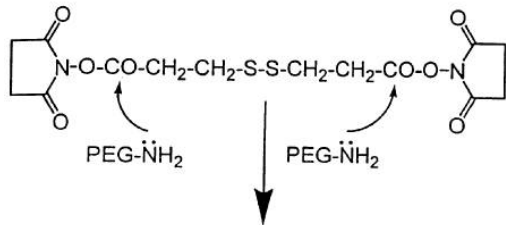
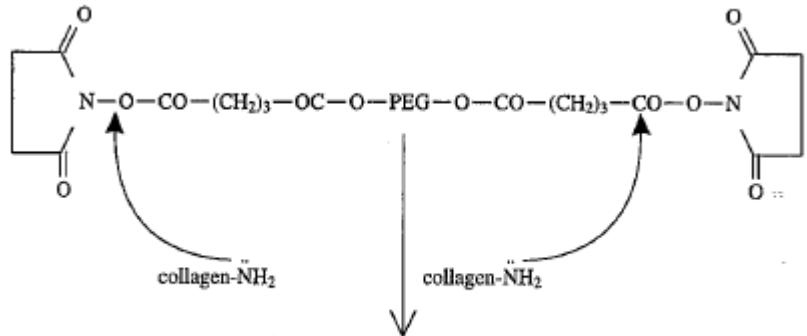
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>KSCN. Reactions were generally allowed to proceed for one hour at 0 °C.</p> <ul style="list-style-type: none"> <u>Dreborg</u>: mPEGOH is suitable for modifying proteins ... Another frequently used method is to couple mPEGOH first to compounds which lead to the introduction of a carboxy group and which can then be activated for final reaction with the <div style="text-align: center;"> <p>Struc 4</p> </div> <p>protein:</p> <p>However, this derivative has an ester linkage which may be hydrolyzed in vivo ...</p> <p>For reaction with proteins, the mPEG acids have been activated in two different ways (e.g., synthesis of hydroxysuccinimide derivative):</p> <div style="text-align: center;"> <p>Struc 7</p> </div> <p>These activated mPEG acids react rapidly with the ε-amino lysine groups as well as with the terminal primary α-amino groups of the proteins. Coupling may also involve the phenolic group of tyrosine and mercapto groups.</p> <ul style="list-style-type: none"> <u>Ellis & Shaikh</u>: cyanoacrylates are both electrophiles and nucleophiles. <u>Fortier et al. Biotechnol. Appl. Biochem.</u> 17 (1993) p.115-130: Five different poly(ethylene glycol)s (PEG) and three different monomethoxypoly(ethylene glycol)s (mPEG), of molecular masses ranging from 750 to 35000, were activated using 4-nitrophenyl chloroformate in acetonitrile in the presence of triethylamine for 5 h at 60°C. This was carried out in order to obtain a high yield of PEG-dinitrophenyl carbonates and mPEG-nitrophenyl carbonates respectively ... It was shown that the formation of the urethane bond between the o-NH2 group of lysine and the activated m/PEG occurred over a wide range of pH and temperature and at various molar ratios of reagents ... mPEGs (M_r values 750, 1900 and 5 000) and PEGs (M_r values 1450, 3 350, 10 000, 20 000 and 35 000) were derivatized using 4-nitrophenyl chloroformate in order to obtain a series of mPEG nitrophenyl carbonates and a series of PEG dinitrophenyl carbonates

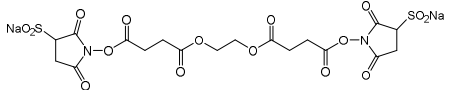
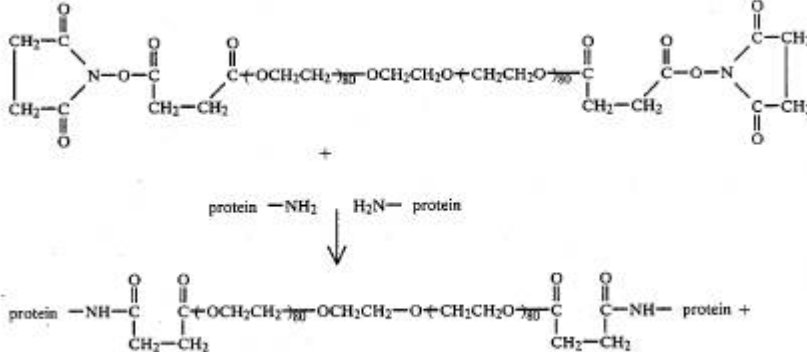
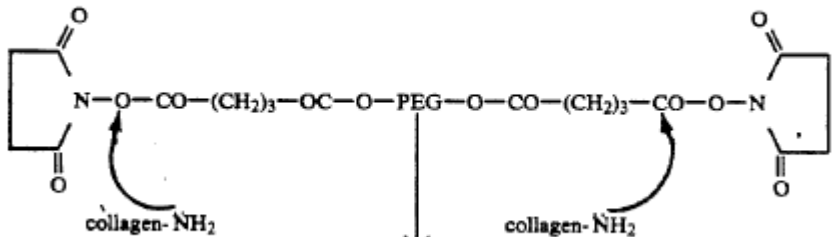
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>respectively ... The modification of HRP was carried out as follows. To 10 mg of HRP, dissolved in 5 ml of 0.1 M borate buffer solution at pH 9.4, was added a corresponding amount of one of the activated PEGs in order to obtain a final free NH₂ groups of HRP /nitrophenyl carbonate groups molar ratio of 1: 4. The reaction mixture was kept at 4 °C overnight under gentle stirring (100 rev./min).</p> <ul style="list-style-type: none"> <u>Larwood & Szoka</u>: Polyethylene glycol diamine 6000 was coupled to methyl p-hydroxybenzimidate, and PEG 1900- and 5000 monomethyl ethers were coupled to tyramine and histamine. <div style="text-align: center;"> <p>6 $\text{MeO}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2\text{OH}$</p> <p>7 $\text{MeO}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{N}-\text{imidazole}$</p> <p>8 $\text{MeO}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{N}-\text{CH}_2\text{CH}_2-\text{R}$ $\text{R} = \text{4-hydroxyphenyl}$</p> <p>9 $\text{R} = \text{1-methyl-1H-imidazol-2-yl}$</p> </div> <ul style="list-style-type: none"> <u>Ulbrich</u>: Diamine PEG-derived nucleophiles disclosed <p style="text-align: center;"> $\text{H}_2\text{NCH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_x-\text{OCH}_2\text{CH}_2\text{NH}_2$ 2 </p>

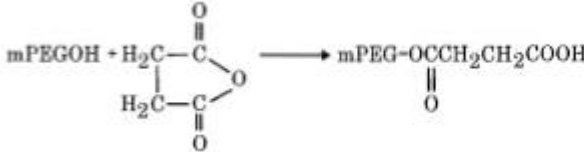
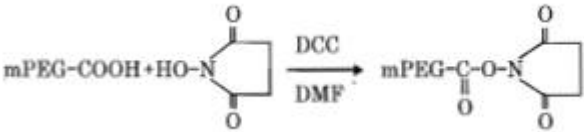
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>crosslinker has nucleophilic functional groups such as amines, the functional polymer may have electrophilic functional groups such as N-hydroxysuccinimides .</p> <ul style="list-style-type: none"> • <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).” BioGlue’s two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds. • <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the Middle Fifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8. $\text{PEG-COO-R-COO-NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG-COO-R-CONH-protein}$ <p><i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.</p> <ul style="list-style-type: none"> • <u>7,279,176</u>: <p>1. Synthesis of copolymer</p> $\begin{array}{c} \text{CH}_2=\text{CHCOO}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2\text{CON} \begin{array}{c} \text{O} \\ \parallel \\ \text{C} \\ \parallel \\ \text{O} \end{array} \text{C}_4\text{H}_6\text{O}_2 + \text{H}_2\text{N}-\text{CH}(\text{CH}_2\text{Cys})-\text{COOH} \longrightarrow \text{ACRL-PEG-Cys} \\ \text{ACRL} \qquad \qquad \text{PEG} \qquad \qquad \text{NHS} \end{array}$

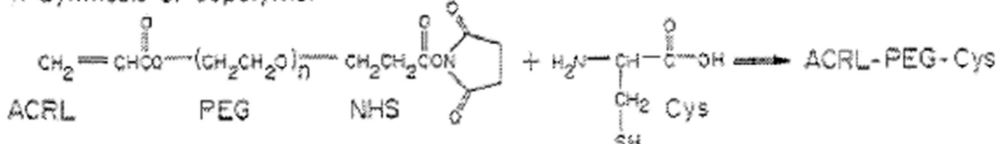
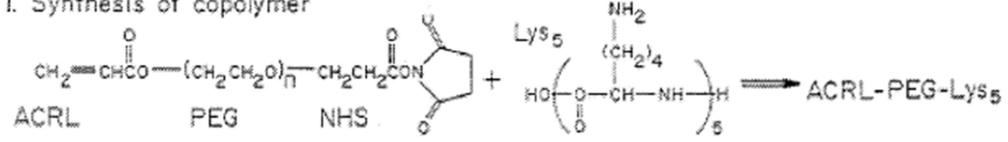
Claim element	Patents in which element is found	Relevant Prior Art References
		<div>1. Synthesis of copolymer</div> <div></div> <ul style="list-style-type: none">• <u>6,162,241</u>: The monomers or macromers preferably include crosslinkable groups which are capable of forming covalent bonds while in aqueous solution. These crosslinkable groups permit crosslinking of the macromers to form a gel. Other crosslinking chemistries which may be used include, for example, reaction of amines or alcohols with isocyanate or isothiocyanate, or of amines or thiols with aldehydes, epoxides, oxiranes, or cyclic imines.• <u>WO 97/22371</u>: Synthetic polymers containing multiple electrophilic groups are also referred to herein as "multi-electrophilic polymers." For use in the present invention, the multifunctionally activated synthetic polymers must contain at least two, more preferably, at least three, electrophilic groups in order to form a three-dimensional crosslinked network with multi-nucleophilic polymers ... Preferred multi-electrophilic polymers for use in the compositions of the invention are polymers which contain two or more succinimidyl groups capable of forming covalent bonds with electrophilic groups on other molecules. Succinimidyl groups are highly reactive with materials containing primary amino (-NH₂) groups, such as multi-amino PEG, poly(lysine), or collagen. Succinimidyl groups are slightly less reactive with materials containing thiol (-SH) groups, such as multi-thiol PEG or synthetic polypeptides containing multiple cysteine residues.• <u>6,371,975</u>: As further defined in this Specification, a "chemically cross-linked" barrier material refers to all barrier materials not formed through the use of enzymes. Cross-linking can occur, e.g., as a result of energy (heat or light), or cross-linking chemical reactions (active esters, isocyanates, epoxides). Examples of these materials includes photo-cross-linked acrylates and nucleophilic attack of electrophiles. The cross-linking group is responsible for the cross-linking of the albumin, as well as the binding to the tissue substrate. The cross-linking group can be selected to selectively react with sulfhydryl groups, selectively react with amines, or can be selected to react with sulfhydryl, primary amino, and secondary amino groups.

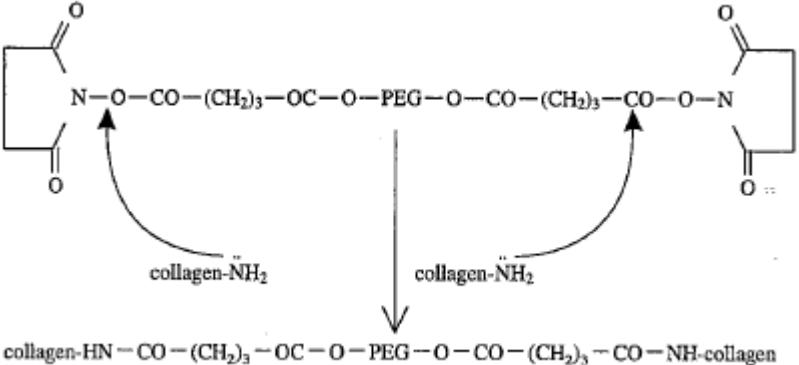
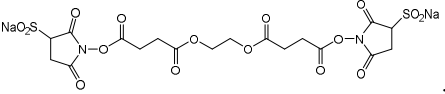
Claim element	Patents in which element is found	Relevant Prior Art References
		<ul style="list-style-type: none">6,458,147: In a preferred embodiment, the material of the covering structure is a protein/polymer composite hydrogel. The material is most preferably formed from the mixture of a protein solution and a solution of an electrophilic derivative of a hydrophilic polymer with a functionality of at least three. The material is nontoxic, biodegradable, and possesses mechanical properties such as cohesive strength, adhesive strength, and elasticity sufficient to block or arrest diffuse organ bleeding, or to block or arrest seepage as a result of anastomosis, or to seal lung punctures. The cross-linking group is responsible for the cross-linking of the albumin, as well as the binding to the tissue substrate. The cross-linking group can be selected to selectively react with sulfhydryl groups, selectively react with amines, or can be selected to react with sulfhydryl, primary amino, and secondary amino groupsBouhadir et al: Otani: In this study, a rapidly curable hydrogel glue was prepared as the seal for lung air leak. Mixing an aqueous solution of gelatin and poly(l-glutamic acid) with a water soluble carbodiimide produced a hydrogel. The mixed gelatin and PLGA aqueous solution sets in several seconds to a hydrogel at 37 °C with the addition of WSC; this is as short as conventional fibrin glue.
Electrophilic groups are	[6,566,406, c8]: The method of claim 7, wherein providing a	<ul style="list-style-type: none">US 6,051,648 (Rhee): A preferred composition of the invention comprises

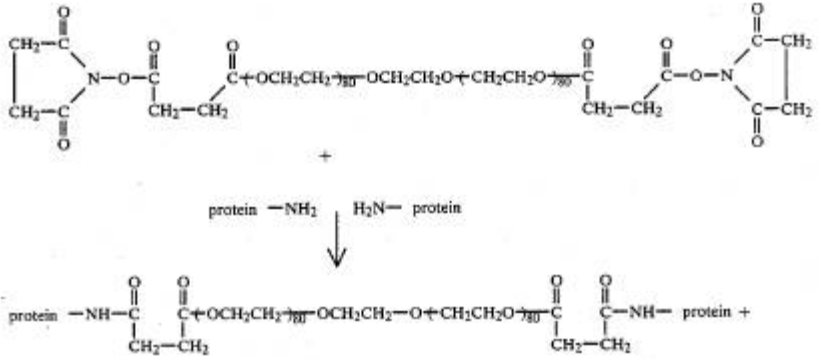
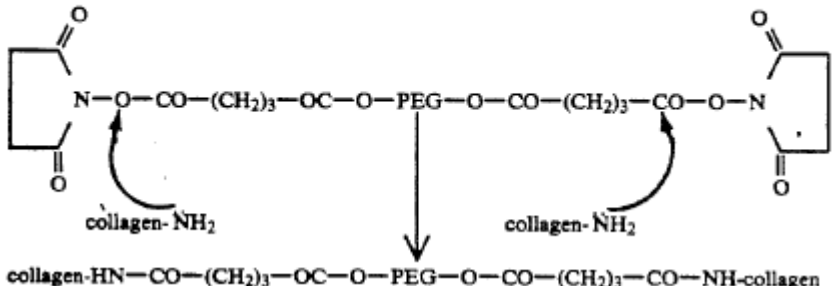
Claim element	Patents in which element is found	Relevant Prior Art References
N-hydroxy succinimide (NHS) groups	<p>synthetic biocompatible functional polymer further comprises providing a synthetic biocompatible functional polymer wherein the functional polymer functional groups are N-hydroxysuccinimide groups.</p> <p>[6,566,406, c18]: The method of claim 17 wherein the first functional groups are the nucleophiles and are amines and the second functional groups are the electrophiles and are succinimides.</p> <p>[8,535,705, c12]: The method of claim 1 wherein the electrophilic functional groups of the first precursor comprise n-hydroxysuccinimide ester.</p>	<p>polyethylene glycol containing two or more primary amino groups as the first synthetic polymer, and polyethylene glycol containing two or more succinimidyl groups (a five-membered ring structure represented herein as --N(COCH₂)₂) as the second synthetic polymer. [note that the succinimidyl groups are indeed N-hydroxy succinimidyl groups as made clear in the Figures].</p> <p>Dithiobis(succinimidylpropionate) (DSP)</p>  <p>PEG-HN-CO-CH₂-CH₂-S-S-CH₂-CH₂-CO-NH-PEG</p> <p>Fig. 15</p> <ul style="list-style-type: none">US 5,614,587 (Rhee): Collagen given as nucleophile  <p>collagen-HN-CO-(CH₂)₃-OC-O-PEG-O-CO-(CH₂)₃-CO-NH-collagen</p> <ul style="list-style-type: none"><u>Prestwich</u>: See Scheme 2: N-hydroxysuccinimide esters are noted as electrophilic in '034. Prestwich teaches substituted NHS esters.

Claim element	Patents in which element is found	Relevant Prior Art References
		<div><p>• <u>4,839,345</u>: NHS esters as electrophilic leaving groups</p><div><p>protein-NH₂ + H₂N-protein</p><p>protein-NH-C(=O)-CH₂-CH₂-C(=O)-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-C(=O)-CH₂-CH₂-C(=O)-NH-protein +</p></div><p>• <u>5,328,955</u>: NHS-groups as electrophilic portion:</p><p>FORMULA 1 S-PEG: Difunctional PEG Succinimidyl Glutarate</p><div><p>collagen-NH₂ + collagen-NH₂</p><p>collagen-HN-CO-(CH₂)₃-OC-O-PEG-O-CO-(CH₂)₃-CO-NH-collagen</p></div><p>• <u>Berger & Pizzo, Blood</u>: Coupling of SS-PEG-5 [<i>i.e., succinimidyl succinate PEG</i>] to rt-PA was carried out at 0.001 to 0.02 mol/L PEG concentrations and 100 ±g/mL rt-PA in 0.1 mol/L potassium phosphate, pH 8.0, containing 1 to 2 mol/L KSCN. Reactions were generally allowed to proceed for one hour at 0 °C.</p><p>• <u>Dreborg</u>: mPEGOH is suitable for modifying proteins ... Another frequently used method is to couple mPEGOH first to compounds which lead to the introduction</p></div>

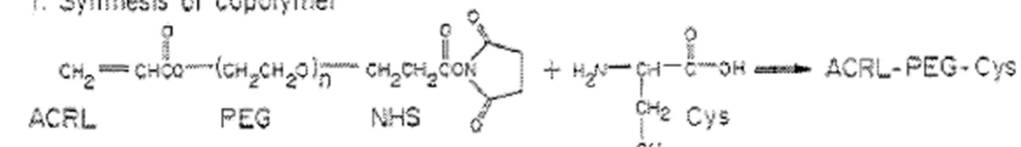
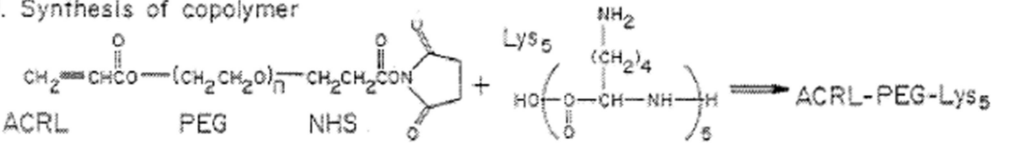
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>of a carboxy group and which can then be activated for final reaction with the</p> <div><p>Struc 4</p></div> <p>protein:</p> <p>However, this derivative has an ester linkage which may be hydrolyzed in vivo ...</p> <p>For reaction with proteins, the mPEG acids have been activated in two different ways (e.g., synthesis of hydroxysuccinimide derivative):</p> <div><p>Struc 7</p></div> <p>These activated mPEG acids react rapidly with the ε-amino lysine groups as well as with the terminal primary α-amino groups of the proteins. Coupling may also involve the phenolic group of tyrosine and mercapto groups.</p> <ul style="list-style-type: none">• <u>WO 2000/09087</u>: Polymerizable groups may be selected from nucleophilic groups and their salts that react further, for example with acylating agents. Useful nucleophilic groups may include amino or thiol groups ... Nucleophilic functional group-containing macromers optionally may be mixed with electrophilic group-containing macromers to rapidly initiate polymerization ... other useful groups include isocyanate, thiocyanate, and N-hydroxy succinimide esters such as succinimide.• <u>WO 2000/033764</u>: Preferably, each precursor comprises only nucleophilic or only electrophilic functional groups, so long as both nucleophilic and electrophilic precursors are used in the crosslinking reaction. Thus, for example, if a crosslinker has nucleophilic functional groups such as amines, the functional polymer may have electrophilic functional groups such as N-hydroxysuccinimides .• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddlesFifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8.</p> <p>$\text{PEG-COO-R-COO-NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG-COO-R-CONH-protein}$</p> <p><i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.</p> <ul style="list-style-type: none">7,279,176:<p>1. Synthesis of copolymer</p><p>1. Synthesis of copolymer</p>WO 97/22371: Synthetic polymers containing multiple electrophilic groups are also referred to herein as "multi-electrophilic polymers." For use in the present invention, the multifunctionally activated synthetic polymers must contain at least two, more preferably, at least three, electrophilic groups in order to form a three- dimensional crosslinked network with multi-nucleophilic polymers ... Preferred multi-electrophilic polymers for use

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>in the compositions of the invention are polymers which contain two or more succinimidyl groups capable of forming covalent bonds with electrophilic groups on other molecules. Succinimidyl groups are highly reactive with materials containing primary amino (-NH₂) groups, such as multi-amino PEG, poly(lysine), or collagen. Succinimidyl groups are slightly less reactive with materials containing thiol (-SH) groups, such as multi-thiol PEG or synthetic polypeptides containing multiple cysteine residues.</p>
<p>Molecular weight of crosslinker is 2,000 or less; crosslinker has two or more electrophilic or nucleophilic functional groups;</p> <p>Second precursor comprises at least 3 nucleophilic functional groups</p>	<p>[6,566,406, c1]: providing a biocompatible small molecule crosslinker with a molecular weight of 2000 or less, the crosslinker having n crosslinker functional groups, wherein n is two or more, and wherein the crosslinker functional groups are either electrophilic or nucleophilic; [6,566,406, c12]</p> <p>[8,535,705, c1]: (ii) the second precursor comprises at least three nucleophilic functional groups;</p>	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: Polyamines such as ethylenediamine (H₂ N--CH₂ CH₂ --NH₂), tetramethylenediamine (H₂ N--(CH₂)₄ --NH₂), pentamethylenediamine (cadaverine) (H₂ N--(CH₂)₅ --NH₂), hexamethylenediamine (H₂ N--(CH₂)₆ --NH₂), bis(2-hydroxyethyl)amine (HN--(CH₂ CH₂ OH)₂), bis(2-aminoethyl)amine (HN--(CH₂ CH₂ NH₂)₂), and tris(2-aminoethyl)amine (N--(CH₂ CH₂ NH₂)₃) may also be used as the synthetic polymer containing multiple nucleophilic groups._• <u>Gayet & Fortier</u>: Reagents are BSA (> 3 nucleophilic groups) and PEG.• <u>US 5,614,587 (Rhee)</u>: Collagen given as nucleophile <div><p>collagen-NH₂</p><p>collagen-NH₂</p><p>collagen-HN-CO-(CH₂)₃-OC-O-PEG-O-CO-(CH₂)₃-CO-NH-collagen</p></div> <ul style="list-style-type: none">• <u>Prestwich</u>: See Scheme 2: N-hydroxysuccinimide esters are noted as electrophilic in '034. The crosslinker below has a molecular weight ~630. <div><p>The corresponding nucleophile is an oligomer of HA with >3 nucleophilic groups.</p></div>

Claim element	Patents in which element is found	Relevant Prior Art References
		<ul style="list-style-type: none">4,839,345: protein nucleophile is understood to have >3 nucleophilic groups <div></div> <ul style="list-style-type: none">5,328,955: at least two NHS-groups as electrophilic portion; collagen understood to have more than three nucleophilic amine residues. <p>FORMULA 1 S-PEG: Difunctional PEG Succinimidyl Glutarate</p> <div></div> <ul style="list-style-type: none">6,165,201: Multifunctional cationic polymers, such as poly(l-lysine), poly(allylamine), poly(ethyleneimine), poly(guanidine), poly(vinyl amine), which contain a plurality of amine functionalities along the backbone, may be used to further induce ionic crosslinks.Berger & Pizzo, Blood: Coupling of SS-PEG-5 [i.e., succinimidyl succinate PEG] to rt-PA was carried out at 0.001 to 0.02 mol/L PEG concentrations and 100 ±g/mL rt-PA in 0.1 mol/L potassium phosphate, pH 8.0, containing 1 to 2 mol/L

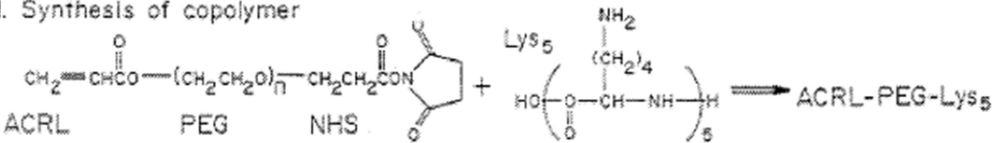
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>KSCN. Reactions were generally allowed to proceed for one hour at 0 °C. [<i>the rt-PA is a protein that has multiple lysine groups</i>].</p> <ul style="list-style-type: none">• <u>Pathak, J.A.C.S.</u> 1992, 114, 8311-8312: Tetrahydroxy PEG (MW 18500) was used ... Other PEGs with MW (400-3500) were α,ω-dihydroxy.• <u>Sawhney et al., Macromolecules</u>, (1993) 26, 581-587: PEGs with molecular weights 1000 (PEG 1K), 4000 (PEG 4K), 6000 (PEG 6K), and 20 000 (PEG 20K) were used.• <u>Ulbrich</u>: Diamine PEG-derived nucleophiles disclosed <p>$\text{H}_2\text{NCH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_x-\text{OCH}_2\text{CH}_2\text{NH}_2$</p> <p style="text-align: center;">2</p> <p>$\text{2} + \text{O}_2\text{N}-\text{C}_6\text{H}_4-\text{O}-\text{CO}-\underset{\text{CH}_2}{\underset{\text{C}_6\text{H}_5}{\text{CH}}}-\text{NH}-\text{CO}-(\text{CH}_2)_4-\text{CO}-\text{NH}-\underset{\text{CH}_2}{\underset{\text{C}_6\text{H}_5}{\text{CH}}}-\text{CO}-\text{O}-\text{C}_6\text{H}_4-\text{NO}_2 \longrightarrow$</p> <p style="text-align: center;">15</p> <p>$\left[\text{CH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_n-\text{OCH}_2\text{CH}_2\text{NH}-\underset{\text{CH}_2}{\underset{\text{C}_6\text{H}_5}{\text{C}}}-\text{NH}-\text{CO}-(\text{CH}_2)_4-\text{CO}-\text{NH}-\underset{\text{CH}_2}{\underset{\text{C}_6\text{H}_5}{\text{C}}}-\text{CO}-\text{NH} \right]_x$</p> <p style="text-align: center;">17</p> <ul style="list-style-type: none">• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).” BioGlue’s two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to

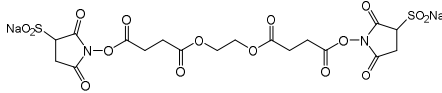
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddlesFifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8.</p> <p>$\text{PEG-COO-R-COO-NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG-COO-R-CONH-protein}$</p> <p><i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.</p> <ul style="list-style-type: none">7,279,176:<p>1. Synthesis of copolymer</p><p>1. Synthesis of copolymer</p>6,162,241: When the reactive group is a reactive group which reacts with only one other group, for example, an isocyanate, then at least some, for example at least about 1%, preferably 2% or more, more typically 5% or more, and optionally up to 100%, of the reactive molecules must contain three or more reactive groups to provide crosslinking. In some chemistries, such as epoxides reacting with primary amines, one group will be mono-reactive (in this example, epoxide) and the other will be multifunctional (in this case, amine, which can react with at least

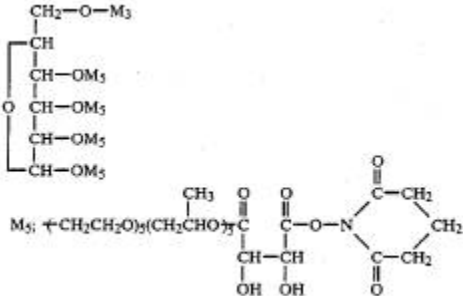
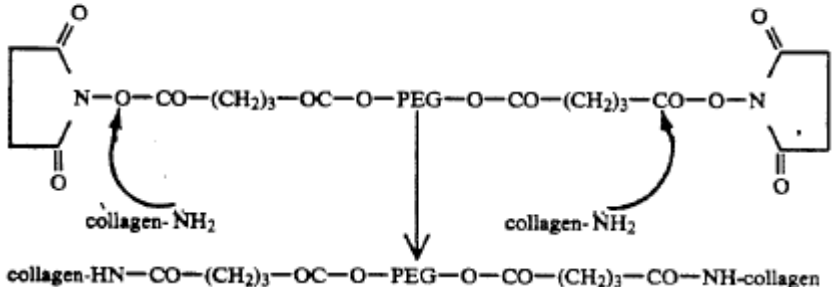
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>two epoxides). In such a reaction, there are several ways in which the required amount of crosslinking can be supplied, with a minimum requirement of some tri-epoxide or some dimeric primary amine.</p> <ul style="list-style-type: none">• <u>WO 97/22371</u>: Japanese patent publication No. 07090241 discloses a composition used for temporary adhesion of a lens material to a support, to mount the material on a machining device, comprising a mixture of polyethylene glycol, having an average molecular weight in the range of 1000 - 5000, and poly-N-vinylpyrrolidone, having an average molecular weight in the range of 30,000 -200,000.• <u>Otani</u>: In this study, a rapidly curable hydrogel glue was prepared as the seal for lung air leak. Mixing an aqueous solution of gelatin and poly(l-glutamic acid) with a water soluble carbodiimide produced a hydrogel. The mixed gelatin and PLGA aqueous solution sets in several seconds to a hydrogel at 37 °C with the addition of WSC; this is as short as conventional fibrin glue.
Small molecule crosslinker has at least 3 functional groups	[6,566,406, c16]: The method of claim 12 wherein the small molecule crosslinker has at least 3 functional groups.	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: Polyamines such as ethylenediamine (H₂ N--CH₂ CH₂ --NH₂), tetramethylenediamine (H₂ N--(CH₂)₄ --NH₂), pentamethylenediamine (cadaverine) (H₂ N--(CH₂)₅ --NH₂), hexamethylenediamine (H₂ N--(CH₂)₆ --NH₂), bis(2-hydroxyethyl)amine (HN--(CH₂ CH₂ OH)₂), bis(2-aminoethyl)amine (HN-(CH₂ CH₂ NH₂)₂), and tris(2-aminoethyl)amine (N--(CH₂ CH₂ NH₂)₃) may also be used as the synthetic polymer containing multiple nucleophilic groups.• <u>Gayet & Fortier</u>: Reagents are BSA (> 3 nucleophilic groups) and PEG.• <u>Prestwich</u>: Scheme 1. Nucleophile bound to Hyaluronic acid is amine (hydrazide): There are multiple (>3) amines along the backbone. <div></div> <ul style="list-style-type: none">• <u>4,839,345</u>: Protein is understood to have >3 nucleophilic groups; Preparation Example 5 shows electrophile with 5 electrophilic groups:

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		<p>The first structure shows a cyclic acetal-protected poly(ethylene glycol) chain with a methyl group at one end. The second structure shows a PEG-succinimidyl glutarate derivative, labeled as Formula 1.</p> <p>M₃: $\text{-(CH}_2\text{CH}_2\text{O)}_3\text{(CH}_2\text{CHO)}_3\text{-C(=O)-CH(OH)-C(=O)-O-N}$ (part of a succinimide ring)</p> <p>FORMULA 1 S-PEG: Difunctional PEG Succinimidyl Glutarate</p> <p>The diagram illustrates the reaction of collagen-NH₂ with S-PEG. The S-PEG molecule consists of two succinimide rings connected by a PEG chain via glutaric acid linkages. Arrows indicate the nucleophilic attack of collagen-NH₂ on the carbonyl carbons of the succinimide rings, leading to the formation of a crosslinked polymer structure where collagen chains are linked by the PEG-S-PEG bridge.</p> <p>collagen-HN-CO-(CH₂)₃-OC-O-PEG-O-CO-(CH₂)₃-CO-NH-collagen</p> <ul style="list-style-type: none"> • <u>5,328,955</u>: at least two NHS-groups as electrophilic portion; collagen understood to have more than three nucleophilic amine residues. • <u>6,165,201</u>: Multifunctional cationic polymers, such as poly(l-lysine), poly(allylamine), poly(ethyleneimine), poly(guanidine), poly(vinyl amine), which contain a plurality of amine functionalities along the backbone, may be used to further induce ionic crosslinks. • Pathak, J.A.C.S. 1992, 114, 8311-8312: Tetrahydroxy PEG (MW 18500) was used ... Other PEGs with MW (400-3500) were α,ω-dihydroxy. • WO 2000/09087: Nucleophilic functional group-containing macromers optionally may be mixed with electrophilic group-containing macromers to rapidly initiate polymerization. It should be noted that several nucleophilic and electrophilic functional groups are naturally present in proteins,

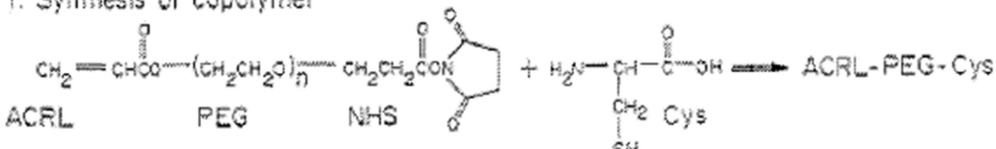
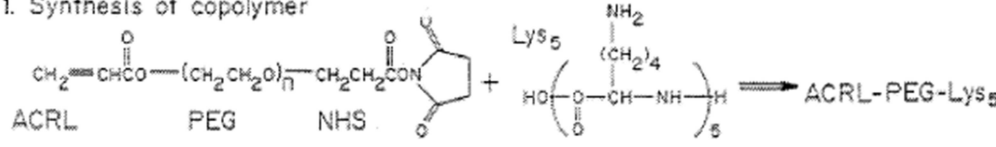
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>polysaccharides, glycosaminoglycans, and oligonucleotides that constitute tissue, cells, and organs and thus both nucleophilic and electrophilic macromers may react with appropriate naturally occurring functional groups in the absence of any additional externally added macromers.</p> <ul style="list-style-type: none">• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddlesFifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8. <p>$\text{PEG-COO-R-COO-NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG-COO-R-CONH-protein}$</p> <ul style="list-style-type: none">• <i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.• <u>7,279,176</u>: <p>1. Synthesis of copolymer</p> <div><div>$\text{CH}_2=\text{CHCOO}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{CH}_2\text{CH}_2\text{CON} \begin{array}{c} \text{O} \\ \parallel \\ \text{C} \end{array} \begin{array}{c} \diagup \diagdown \\ \text{O} \quad \text{O} \end{array}$<div>ACRLPEGNHS</div></div><div>$+ \text{H}_2\text{N}-\text{CH}(\text{CH}_2\text{Cys})-\text{COOH} \rightarrow \text{ACRL-PEG-Cys}$<div>Cys</div></div></div>

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>1. Synthesis of copolymer</p> <div></div> <ul style="list-style-type: none">• <u>6,162,241</u>: When the reactive group is a reactive group which reacts with only one other group, for example, an isocyanate, then at least some, for example at least about 1%, preferably 2% or more, more typically 5% or more, and optionally up to 100%, of the reactive molecules must contain three or more reactive groups to provide crosslinking. In some chemistries, such as epoxides reacting with primary amines, one group will be mono-reactive (in this example, epoxide) and the other will be multifunctional (in this case, amine, which can react with at least two epoxides). In such a reaction, there are several ways in which the required amount of crosslinking can be supplied, with a minimum requirement of some tri-epoxide or some dimeric primary amine.• <u>WO 97/22371</u>: Synthetic polymers containing multiple nucleophilic groups are also referred to generically herein as "multi-nucleophilic polymers". For use in the present invention, multi-nucleophilic polymers must contain at least two, more preferably, at least three, nucleophilic groups. If a synthetic polymer containing only two nucleophilic groups is used, a synthetic polymer containing three or more electrophilic groups must be used in order to obtain a three-dimensional crosslinked network ... Preferred multi-nucleophilic polymers include: (i) synthetic polypeptides that have been synthesized to contain two or more primary amino groups or thiol groups; and (ii) polyethylene glycols that have been modified to contain two or more primary amino groups or thiol groups.• <u>WO 97/22371</u>: Synthetic polymers containing multiple electrophilic groups are also referred to herein as "multi-electrophilic polymers." For use in the present invention, the multifunctionally activated synthetic polymers must contain at least two, more preferably, at least three, electrophilic groups in order to form a three- dimensional crosslinked network with

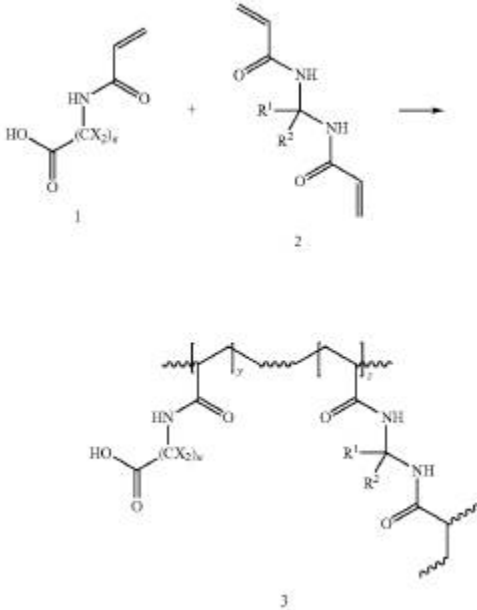
Claim element	Patents in which element is found	Relevant Prior Art References
		multi-nucleophilic polymers ... Preferred multi-electrophilic polymers for use in the compositions of the invention are polymers which contain two or more succinimidyl groups capable of forming covalent bonds with electrophilic groups on other molecules. Succinimidyl groups are highly reactive with materials containing primary amino (-NH ₂) groups, such as multi-amino PEG, poly(lysine), or collagen. Succinimidyl groups are slightly less reactive with materials containing thiol (-SH) groups, such as multi-thiol PEG or synthetic polypeptides containing multiple cysteine residues.
Hydrogel is made of synthetic materials	[7,009,034, c3]: The method of claim 1, wherein the hydrogel is made of synthetic materials.	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: In accordance with the present invention, crosslinked polymer compositions are prepared by reacting a first synthetic polymer containing two or more nucleophilic groups with a second synthetic polymer containing two or more electrophilic groups capable of covalently binding with the nucleophilic groups on the first synthetic polymer.• <u>Tse</u>: cyanoacrylate is synthetic material.• <u>US 5,614,587 (Rhee)</u>: The present invention discloses compositions suitable for use as bioadhesives, which compositions comprise fibrillar collagen, a fiber disassembly agent, and a multifunctionally activated synthetic hydrophilic polymer,• <u>Gayet & Fortier</u>: Reagents are BSA (> 3 nucleophilic groups) and PEG (synthetic material).• <u>Prestwich</u>: See the electrophilic portion is clearly synthetic. The HA-based (nucleophilic) precursor is made by synthesis – reacting HA with hydrazide <div></div> <ul style="list-style-type: none">• <u>2014/0243428</u>: Synthetic monomers: Monomers N-acryloyl 2-glycine (A2AGA), N-acryloyl 4-aminobutyric acid (A4ABA), N-acryloyl 6-aminocaproic acid (A6ACA), N-acryloyl 8-aminocaprylic acid (A8ACA), and N-acryloyl 11-aminoundecanoic acid (A11AUA) were synthesized from glycine (Fisher Scientific, Inc.), 4-aminobutyric acid, 6-aminocaproic acid, 8-aminocaprylic acid (Acros Organics, Inc.), and 11-aminoundecanoic acid (Aldrich), respectively, as is described in Ayala, et al., <i>Biomaterials</i> (2011) 32:3700-3711, which is

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>incorporated herein in its entirety.</p> <ul style="list-style-type: none">4,839,345: Electrophiles are made synthetically by conversion to NHS esters: 5,328,955: PEG is a synthetic material. <p>FORMULA 1</p><p>S-PEG: Difunctional PEG Succinimidyl Glutarate</p>6,165,201: Solutions of other synthetic polymers such as poly(N-alkylacrylamides) also form hydrogels that exhibit thermoreversible behavior and exhibit weak physical crosslinks on warmingChampagne: cyanoacrylates are synthetic.Ellis & Shaikh: cyanoacrylates are both electrophiles and nucleophiles and are synthetic.Fortier et al. Biotechnol. Appl. Biochem. 17 (1993) p.115-130: Five different poly(ethylene glycol)s (PEG) and three different monomethoxypoly(ethylene glycol)s (mPEG), of molecular masses ranging from 750 to 35000, were activated

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>using 4-nitrophenyl chloroformate in acetonitrile in the presence of triethylamine for 5 h at 60°C. This was carried out in order to obtain a high yield of PEG-dinitrophenyl carbonates and mPEG-nitrophenyl carbonates respectively ... It was shown that the formation of the urethane bond between the o-NH2 group of lysine and the activated m/PEG occurred over a wide range of pH and temperature and at various molar ratios of reagents ... mPEGs (M_r values 750, 1900 and 5 000) and PEGs (M_r values 1450, 3 350, 10 000, 20 000 and 35 000) were derivatized using 4-nitrophenyl chloroformate in order to obtain a series of mPEG nitrophenyl carbonates and a series of PEG dinitrophenyl carbonates respectively ... The modification of HRP was carried out as follows. To 10 mg of HRP, dissolved in 5 ml of 0.1 M borate buffer solution at pH 9.4, was added a corresponding amount of one of the activated PEGs in order to obtain a final free NH2 groups of HRP /nitrophenyl carbonate groups molar ratio of 1: 4. The reaction mixture was kept at 4 °C overnight under gentle stirring (100 rev./min).</p> <ul style="list-style-type: none">• <u>Pathak, J.A.C.S.</u> 1992, 114, 8311-8312: Tetrahydroxy PEG (MW 18500) was used ... Other PEGs with MW (400-3500) were α,ω-dihydroxy.• <u>Sawhney et al., Macromolecules</u>, (1993) 26, 581-587: Macromers having a poly(ethylene glycol) central block, extended with oligomers of α-hydroxy acids such as oligo(dl-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation of cross-linked gels. These gels degrade upon hydrolysis of the oligo(α-hydroxy acid) regions into poly(ethylene glycol), the α-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular drug delivery.• <u>Ulbrich</u>: Diamine PEG-derived nucleophiles disclosed <p>H₂NCH₂CH₂-(OCH₂CH₂)_x-OCH₂CH₂NH₂</p> <p>2</p>

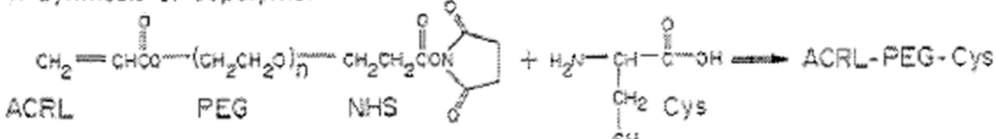
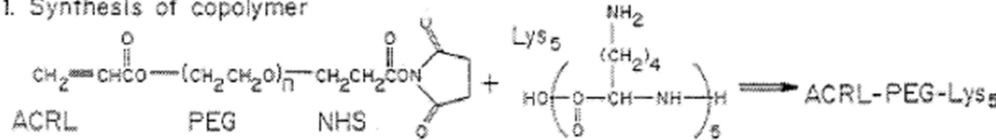
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8.</p> <p>$\text{PEG-COO-R-COO-NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG-COO-R-CONH-protein}$</p> <p><i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.</p> <ul style="list-style-type: none">• <u>Davis</u>: Teaches “medical version of super glue” comprises cyanoacrylates that are simultaneously nucleophile and electrophile.• <u>7,279,176</u>:<ol style="list-style-type: none">1. Synthesis of copolymer<div></div><ol style="list-style-type: none">1. Synthesis of copolymer<div></div><ul style="list-style-type: none">• <u>WO 97/22371</u>: Synthetic polymers containing multiple nucleophilic groups are also referred to generically herein as "multi-nucleophilic polymers". For use in the present invention, multi-nucleophilic polymers must contain at least two, more preferably, at least three, nucleophilic groups. If a synthetic polymer containing only two nucleophilic groups is used, a synthetic polymer containing three or more electrophilic groups must be used in order to obtain a three-dimensional crosslinked network ... Preferred multi-nucleophilic polymers include: (i) synthetic polypeptides that have been synthesized to contain two or more primary amino groups or thiol groups; and (ii) polyethylene glycols that have been modified to contain two or more primary amino groups or thiol groups.

Claim element	Patents in which element is found	Relevant Prior Art References
		<ul style="list-style-type: none"> • <u>WO 97/22371</u>: Synthetic polymers containing multiple electrophilic groups are also referred to herein as "multi-electrophilic polymers." For use in the present invention, the multifunctionally activated synthetic polymers must contain at least two, more preferably, at least three, electrophilic groups in order to form a three-dimensional crosslinked network with multi-nucleophilic polymers ... Preferred multi-electrophilic polymers for use in the compositions of the invention are polymers which contain two or more succinimidyl groups capable of forming covalent bonds with electrophilic groups on other molecules. Succinimidyl groups are highly reactive with materials containing primary amino (-NH₂) groups, such as multi-amino PEG, poly(lysine), or collagen. Succinimidyl groups are slightly less reactive with materials containing thiol (-SH) groups, such as multi-thiol PEG or synthetic polypeptides containing multiple cysteine residues. • <u>6,371,975</u>: In a preferred embodiment of the invention, the barrier material loses its physical strength during the first twenty days, and total resorption occurs in about 4 weeks. • <u>Otani</u>: In this study, a rapidly curable hydrogel glue was prepared as the seal for lung air leak. Mixing an aqueous solution of gelatin and poly(l-glutamic acid) with a water soluble carbodiimide produced a hydrogel. The mixed gelatin and PLGA aqueous solution sets in several seconds to a hydrogel at 37 °C with the addition of WSC; this is as short as conventional fibrin glue.
Hydrogel comprises covalently crosslinked hydrophilic polymers	[7,009,034, c5]: The method of claim 1, wherein the hydrogel comprises covalently crosslinked hydrophilic polymers.	<ul style="list-style-type: none"> • <u>US 6,051,648 (Rhee)</u>: This invention relates generally to crosslinked polymer compositions ... FIGS. 4 to 13 show the formation of various crosslinked synthetic polymer compositions from hydrophilic polymers ... Hydrophilic polymers and, in particular, various polyethylene glycols, are preferred for use in the compositions of the present invention. As used herein, the term "PEG" refers to polymers having the repeating structure (OCH₂ CH₂)_n. • <u>US 5,614,587 (Rhee)</u>: A composition comprising fibrillar collagen, a biocompatible alcohol, and a multifunctionally activated synthetic hydrophilic polymer, wherein the biocompatible alcohol is present in an amount sufficient to render the collagen substantially nonfibrillar at pH 7, and wherein the collagen

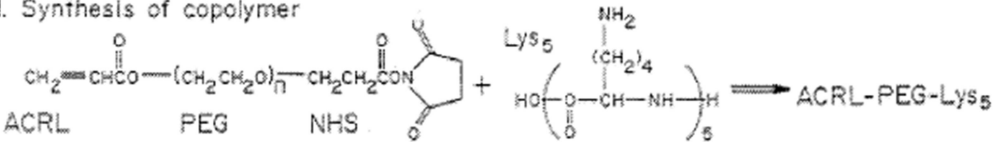
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>and synthetic polymer covalently bind to form a collagen--synthetic polymer conjugate</p> <ul style="list-style-type: none">• <u>Gayet & Fortier</u>: Reagents are BSA (> 3 nucleophilic groups) and PEG (hydrophilic polymer).• <u>Prestwich</u>: functionalized HA was dissolved in water at 15 mg/mL.• <u>2014/0243428</u>: See scheme 1: covalent crosslinking: <div></div> <ul style="list-style-type: none">• <u>4,839,345</u>: Proteins (nucleophiles) are water-soluble; PEG (electrophiles) is water soluble.• <u>5,328,955</u>: Scheme 1 shows covalently crosslinked hydrogel.

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>FORMULA 1</p> <p>S-PEG: Difunctional PEG Succinimidyl Glutarate</p> <p>$\text{collagen-NH}_2 + \text{S-PEG} + \text{collagen-NH}_2 \rightarrow \text{collagen-HN-CO-(CH}_2\text{)}_3\text{-OC-O-PEG-O-CO-(CH}_2\text{)}_3\text{-CO-NH-collagen}$</p> <ul style="list-style-type: none">• <u>6,165,201</u>: Preferably, the solutions are substantially soluble in water to allow application in a physiologically-compatible solution, such as buffered isotonic saline. Water-soluble coatings may form thin films, but more preferably form three-dimensional gels of controlled thickness.• <u>Pathak, J.A.C.S. 1992, 114, 8311-8312</u>: Tetrahydroxy PEG (MW 18500) was used ... Other PEGs with MW (400-3500) were α,ω-dihydroxy.• <u>Sawhney et al., Macromolecules, (1993) 26, 581-587</u>: Macromers having a poly(ethylene glycol) central block, extended with oligomers of α-hydroxy acids such as oligo(dl-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation of cross-linked gels. These gels degrade upon hydrolysis of the oligo(α-hydroxy acid) regions into poly(ethylene glycol), the α-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular drug delivery.• <u>Ulbrich</u>: Diamine PEG-derived nucleophiles disclosed

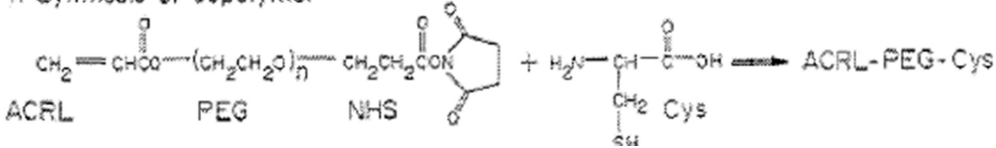
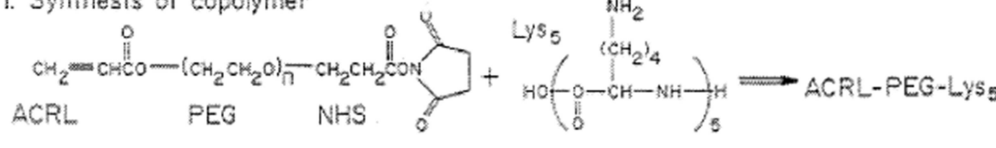
Claim element	Patents in which element is found	Relevant Prior Art References
		<div><p>$\text{H}_2\text{NCH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_x-\text{OCH}_2\text{CH}_2\text{NH}_2$<p style="text-align: center;">2</p><p>$\text{2} + \text{O}_2\text{N}-\text{C}_6\text{H}_4-\text{O}-\text{CO}-\underset{\text{CH}_2}{\underset{\text{C}_6\text{H}_5}{\text{CH}}}-\text{NH}-\text{CO}-(\text{CH}_2)_4-\text{CO}-\text{NH}-\underset{\text{CH}_2}{\underset{\text{C}_6\text{H}_5}{\text{CH}}}-\text{CO}-\text{O}-\text{C}_6\text{H}_4-\text{NO}_2 \longrightarrow$<p style="text-align: center;">15</p><p>$\left[\text{CH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2)_n-\text{OCH}_2\text{CH}_2\text{NH}-\underset{\text{CH}_2}{\underset{\text{C}_6\text{H}_5}{\text{C}}}(\text{O})-\text{CH}-\text{NH}-\text{CO}-(\text{CH}_2)_4-\text{CO}-\text{NH}-\underset{\text{CH}_2}{\underset{\text{C}_6\text{H}_5}{\text{C}}}(\text{O})-\text{NH} \right]_x$<p style="text-align: center;">17</p></p></p></p></div> <ul style="list-style-type: none">• <u>WO 2000/09087</u>: Other useful electrophilic macromers may contain functional groups such as glycidyl ethers (or epoxides) or hydroxyl group containing polymers that have been activated with 1, 1, -carbonyl diimidazole (for example PEG-oxycarbonylimidazole) or p-nitrophenyl chlorocarbonates (e.g., PEG nitrophenyl carbonate), tresylates, aldehydes and isocyanates.• <u>WO 2000/033764</u>: Each precursor is multifunctional, meaning that it comprises two or more electrophilic or nucleophilic functional groups, such that a nucleophilic functional group on one precursor may react with an electrophilic functional group on another precursor to form a covalent bond.• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an

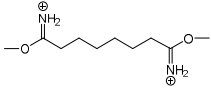
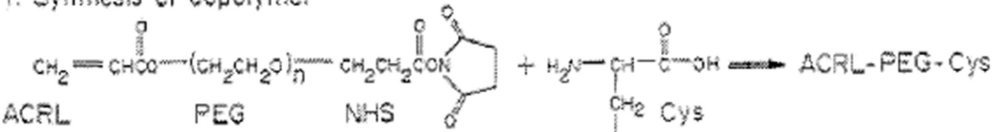
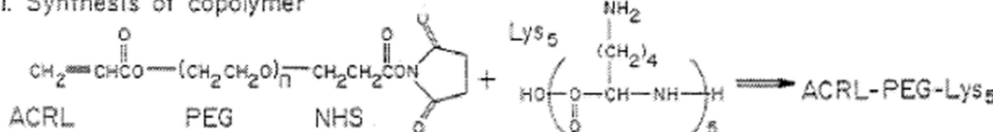
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the Middle Fifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8.</p> <p>$\text{PEG}-\text{COO}-\text{R}-\text{COO}-\text{NHS} + \text{NH}_2\text{-protein} \rightarrow$</p> <p>$\text{PEG}-\text{COO}-\text{R}-\text{CONH}-\text{protein}$</p> <ul style="list-style-type: none">• <i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.• <u>Davis</u>: Teaches “medical version of super glue” comprises cyanoacrylates that are simultaneously nucleophile and electrophile. Form covalent bonds• <u>7,279,176</u>:<ol style="list-style-type: none">1. Synthesis of copolymer<div></div><ol style="list-style-type: none">1. Synthesis of copolymer<div></div>• <u>WO 97/22371</u>: Hydrophilic polymers and, in particular, various polyethylene glycols, are preferred for use in the compositions of the present invention. As used herein, the term "PEG" refers to polymers having the repeating structure (OCH2CH2)n.• <u>Miranda</u>: The process of drying a complex mixture of macromolecules like PVP, PEG and agar showed an irreversible behavior upon hydration, probably as a

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>function of physical crosslinking.</p> <ul style="list-style-type: none">• <u>Russell</u>: simple approach is described for preparing poly-(ethylene glycol) hydrogel materials with encapsulated seminaphthofluorescein (SNAFL)-organophosphorus hydrolase enzyme conjugates.
Functional polymer weighs more than 7x as much as the crosslinker, with 2 or more functional groups (m + n ≥ 5)	<p>[6,566,406, c1]: providing a synthetic biocompatible functional polymer with a molecular weight of at least about 7 times more than the crosslinker, the functional polymer having m functional polymer functional groups, wherein m is two or more and the sum of n and m functional polymer functional groups, wherein m is two or more and the sum of n and m is five or more, and wherein the functional polymer functional groups are nucleophilic if the crosslinker functional groups are electrophilic, and the functional polymer functional groups are electrophilic if the crosslinker functional groups are nucleophilic; and</p> <p>[6,566,406, c12]</p>	<ul style="list-style-type: none">• <u>US 5,614,587 (Rhee)</u>: Example 1 uses SG-PEG (MW 3800). MW of collagen is ~115 to 130kDa• <u>Gayet & Fortier</u>: BSA (~66 kDa); PEG (3350 Da)• <u>Prestwich</u>: Teaches ~630 MW crosslinker with a functionalized hyaluronate (MW~ 1.5 x 10⁶).• <u>5,328,955</u>: teaches collagen can be modified by acid and enzymatic digestion to make it less immunogenic than native collagen (Daniels et al U.S. Pat. No. 3,949,073). The term "collagen" as used herein refers to all forms of collagen, including those which have been processed or otherwise modified. Example 1C teaches crosslinking collagen with PEG 3400. The collagen used is pepsin extracted Vitrogen 100.• <u>Pathak, J.A.C.S. 1992, 114, 8311-8312</u>: Tetrahydroxy PEG (MW 18500) was used ... Other PEGs with MW (400-3500) were α,ω-dihydroxy.• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>7,279,176</u>: 1. Synthesis of copolymer

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>1. Synthesis of copolymer</p> <div></div> <ul style="list-style-type: none">• <u>WO 97/22371</u>: Japanese patent publication No. 07090241 discloses a composition used for temporary adhesion of a lens material to a support, to mount the material on a machining device, comprising a mixture of polyethylene glycol, having an average molecular weight in the range of 1000 - 5000, and poly-N-vinylpyrrolidone, having an average molecular weight in the range of 30,000 -200,000.
Synthetic polymer weighs about 20 times the molecular weight of the crosslinker	[6,566,406, c26]: The crosslinked biocompatible material of claim 23 wherein the synthetic polymer molecular weight is at least about 20 times the molecular weight of the crosslinker.	<ul style="list-style-type: none">• <u>US 5,614,587 (Rhee)</u>: Example 1 uses SG-PEG (MW 3800). MW of collagen is ~115 to 130kDa• <u>Prestwich</u>: Teaches ~630 MW crosslinker with a functionalized hyaluronate (MW~ 1.5 x 10⁶).• <u>5,328,955</u>: teaches collagen can be modified by acid and enzymatic digestion to make it less immunogenic than native collagen (Daniels et al U.S. Pat. No. 3,949,073). The term "collagen" as used herein refers to all forms of collagen, including those which have been processed or otherwise modified. Example 1C teaches crosslinking collagen with PEG 3400. The collagen used is pepsin extracted Vitrogen 100.• <u>Pathak, J.A.C.S. 1992, 114, 8311-8312</u>: Tetrahydroxy PEG (MW 18500) was used ... Other PEGs with MW (400-3500) were α,ω-dihydroxy.• <u>WO 2000/033764</u>: While these electrophilic-nucleophilic polymerization methods do not suffer from the same limitations as free radical polymerization methods, described above, they have other limitations stemming from their use of polymeric precursors. Mixing can be a significant impediment to such reactions since polymeric precursors are often of a higher viscosity and diffusion is impeded, especially with the onset of gelation. Thus, imperfections in the crosslinked structures and weaknesses may result. In contrast, the use of at least

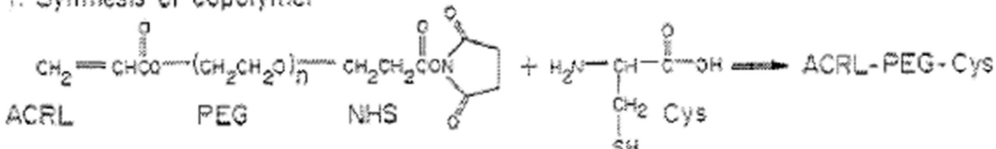
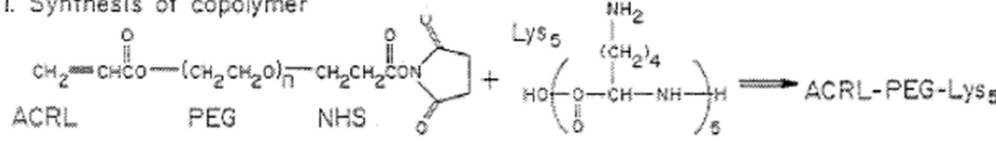
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>one small molecule precursor (where small molecule refers to a molecule that is not a polymer and is typically of a molecular weight less than 2000 Daltons, or else is a polymer and is of a molecular weight of less than 1000 Daltons) allows for diffusion of the small molecule throughout the crosslinked structure, even after gelation, and thus may result in superior materials.</p> <ul style="list-style-type: none">• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).” BioGlue’s two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>7,279,176</u>: 1. Synthesis of copolymer 1. Synthesis of copolymer <ul style="list-style-type: none">• <u>WO 97/22371</u>: Japanese patent publication No. 07090241 discloses a composition used for temporary adhesion of a lens material to a support, to mount the material on a machining device, comprising a mixture of polyethylene glycol, having an average molecular weight in the range of 1000 - 5000, and poly-N-vinylpyrrolidone, having an average molecular weight in the range of 30,000 -200,000.
Second and third precursors have molecular weight less than about 1000.	[8,003,705, c5]: The kit of claim 4 wherein the second biocompatible precursor and the third biocompatible precursor each have a molecular weight of less than about 1000. [8,003,705, c12]	<ul style="list-style-type: none">• <u>Prestwich</u>: Teaches multiple crosslinkers with MW ~630 or less.• <u>Pathak, J.A.C.S.</u> 1992, 114, 8311-8312: Tetrahydroxy PEG (MW 18500) was used ... Other PEGs with MW (400-3500) were α,ω-dihydroxy.• <u>Sawhney et al., Macromolecules</u>, (1993) 26, 581-587: PEGs with molecular

Claim element	Patents in which element is found	Relevant Prior Art References
	[8,535,705, c9]: The method of claim 1 wherein the second precursor has a molecular weight of less than about 1000 Daltons.	<p>weights 1000 (PEG 1K), 4000 (PEG 4K), 6000 (PEG 6K), and 20 000 (PEG 20K) were used.</p> <ul style="list-style-type: none">• <u>WO 2000/033764</u>: While these electrophilic-nucleophilic polymerization methods do not suffer from the same limitations as free radical polymerization methods, described above, they have other limitations stemming from their use of polymeric precursors. Mixing can be a significant impediment to such reactions since polymeric precursors are often of a higher viscosity and diffusion is impeded, especially with the onset of gelation. Thus, imperfections in the crosslinked structures and weaknesses may result. In contrast, the use of at least one small molecule precursor (where small molecule refers to a molecule that is not a polymer and is typically of a molecular weight less than 2000 Daltons, or else is a polymer and is of a molecular weight of less than 1000 Daltons) allows for diffusion of the small molecule throughout the crosslinked structure, even after gelation, and thus may result in superior materials.• <u>7,279,176</u>: 1. Synthesis of copolymer  1. Synthesis of copolymer • <u>WO 97/22371</u>: Japanese patent publication No. 07090241 discloses a composition used for temporary adhesion of a lens material to a support, to mount the material on a machining device, comprising a mixture of polyethylene glycol, having an average molecular weight in the range of 1000 - 5000, and poly-N-vinylpyrrolidone, having an average molecular weight in the range of 30,000 -200,000.•

Claim element	Patents in which element is found	Relevant Prior Art References
Crosslinker has a molecular weight of 100 to 200 when not bonded to the polymer	[6,566,406, c19]: with the crosslinker having a water solubility of at least 1 gram per 100 milliliters and being of a molecular weight of 100 to 2000 when not bonded to the polymer; and	<div></div> <ul style="list-style-type: none">• <u>Prestwich</u>:• <u>7,279,176</u>: <p>1. Synthesis of copolymer</p> <div></div> <p>1. Synthesis of copolymer</p> <div></div> <ul style="list-style-type: none">•
Nature of second precursor	[8,003,705, c1]: wherein the second precursor is a member of the group consisting of ornithine, spermine, spermidine, urea, guanidine, dianmiopimelic acid, diaminobutyric acid, methylornithine, diaminopropionic acid, cystine, lanthionine, cystamine, trioxatridecanediamine, cyclohexanebis(methylamine), tetraethylenepentamine, pentaethylenehexamine, methylenebis(methylcyclohexamine), diaminocyclohexane, n-(2-aminoethyl)-1,3-propanediamine, diaminomethyldipropylamine, iminobispropylamine, bis(hexamethylene)triamine, triethylenetetramine, bis(aminopropyl)ethylenediamine, bis(2-aminoethyl)-1,3-propanediamine, bis(aminopropyl)propanediamine, diamniomethylpropane, 1,2-diamino-2-methylpropane, 1,3-diaminopentane, dimethylpropanediamine, 2,2-dimethyl 1,3-propanediamine, methylpentanediamine, 2-methyl-1,5 pentanediamine, diaminoheptane, diaminooctane, diaminononane, and diaminododecane.	<ul style="list-style-type: none">• <u>US 5,658,592</u>: The salt of the crosslinking reagent represented by the general formula (II) specifically includes the salts of diaminoalkanes such as diaminoethane, diaminopropane, diaminobutane, diaminopentane, diaminohexane, diaminoheptane, diaminooctane, diaminononane, diaminodecane, diaminododecane, diaminooctadecane, etc

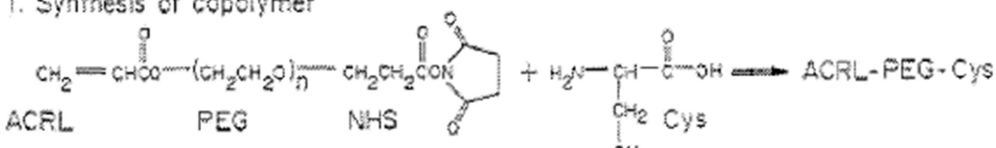
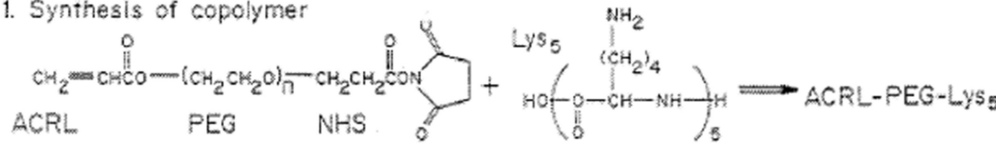
Claim element	Patents in which element is found	Relevant Prior Art References
A third biocompatible precursor	[8,003,705, c4]: a third biocompatible precursor comprising at least two primary amine functional groups	<ul style="list-style-type: none"> • <u>US 5,614,587 (Rhee)</u>: Collagen is inherently a mixture of different molecules of differing molecular weights. • <u>Gayet & Fortier</u>: PEG is inherently a mixture of different molecules of differing molecular weights. • <u>Prestwich</u>: Modified HA is a mixture of different molecules of differing molecular weights. • <u>5,328,955</u>: Collagen is inherently a mixture of different molecules of differing molecular weights. Same applies to PEG distributions. • <u>WO 2000/09087</u>: it is also understood that more than one type of electrophilic group or nucleophilic group may be present as a part of a macromere chain, so that multiple levels of reactivities may be built into the materials.
Solubility of small molecule crosslinker is \geq 1 g/100 mL water	<p>[6,566,406, c2]: The method of claim 1, wherein providing a biocompatible small molecule crosslinker further comprises providing a biocompatible small molecule crosslinker having a solubility of at least 1 g/100 ml in an aqueous solution.</p> <p>[8,535,705, c1]: with the first biocompatible synthetic hydrophilic polymer precursor having a water solubility of at least 1 gram per 100 milliliters and comprising at least two electrophilic functional groups;</p>	<ul style="list-style-type: none"> • <u>US 6,051,648 (Rhee)</u>: FIGS. 4 to 13 show the formation of various crosslinked synthetic polymer compositions from hydrophilic polymers ... Hydrophilic polymers and, in particular, various polyethylene glycols, are preferred for use in the compositions of the present invention. As used herein, the term "PEG" refers to polymers having the repeating structure $(\text{OCH}_2 \text{CH}_2)_n$. [<i>PEG is known to be miscible with water</i>]. • <u>US 6,051,648 (Rhee)</u>: See Example 1; final concentration of collagen in samples is 18 mg/mL; SG-PEG in PBS at 100 mg/mL • <u>Gayet & Fortier</u>: PEG is water-soluble • <u>Prestwich</u>: Modified HA dissolved in water at 15 mg/mL. Disclosure also teaches charged crosslinkers that would likely be miscible in water. • <u>4,839,345</u>: Proteins (nucleophiles) are water-soluble; PEG (electrophiles) is water soluble. • <u>5,328,955</u>: PEG is soluble in water. Vitrogen collagen is now sold as "Bovine Collagen Solution, Type I, 3 mg/ml, 100 ml" • <u>6,165,201</u>: Preferably, the solutions are substantially soluble in water to allow application in a physiologically-compatible solution, such as buffered isotonic saline. Water-soluble coatings may form thin films, but more preferably form three-dimensional gels of controlled thickness.

Claim element	Patents in which element is found	Relevant Prior Art References
		<ul style="list-style-type: none">• <u>Pathak, J.A.C.S.</u> 1992, 114, 8311-8312: Tetrahydroxy PEG (MW 18500) was used ... Other PEGs with MW (400-3500) were α,ω-dihydroxy. PEG is water soluble.• <u>Sawhney et al., Macromolecules</u>, (1993) 26, 581-587: Macromers having a poly(ethylene glycol) central block, extended with oligomers of α-hydroxy acids such as oligo(dl-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation of cross-linked gels. These gels degrade upon hydrolysis of the oligo(α-hydroxy acid) regions into poly(ethylene glycol), the α-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular drug delivery.• <u>WO 2000/09087</u>: Other useful electrophilic macromers may contain functional groups such as glycidyl ethers (or epoxides) or hydroxyl group containing polymers that have been activated with 1, 1, -carbonyl diimidazole (for example PEG-oxycarbonylimidazole) or p-nitrophenyl chlorocarbonates (e.g., PEG nitrophenyl carbonate), tresylates, aldehydes and isocyanates.• <u>WO 2000/033764</u>: More preferably, the crosslinker has a solubility of at least 1 g/100 mL in an aqueous solution• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddleFifty milligrams

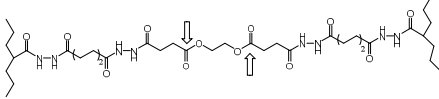
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8.</p> <p>$\text{PEG-COO-R-COO-NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG-COO-R-CONH-protein}$</p> <ul style="list-style-type: none">• <i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.• <u>7,279,176</u>:<ol style="list-style-type: none">1. Synthesis of copolymer 1. Synthesis of copolymer • <u>WO 97/22371</u>: Hydrophilic polymers and, in particular, various polyethylene glycols, are preferred for use in the compositions of the present invention. As used herein, the term "PEG" refers to polymers having the repeating structure (OCH₂CH₂)_n.• <u>Russell</u>: simple approach is described for preparing poly-(ethylene glycol) hydrogel materials with encapsulated seminaphthofluorescein (SNAFL)-organophosphorus hydrolase enzyme conjugates.
Concentration of solids in the hydrogel is about 8-20	[6,566,406, c16]: The method of claim 16 wherein the concentration of solids in the hydrogel is about 8-20 percent.	<ul style="list-style-type: none">• <u>6,051,648</u>: 0.15 grams of di-amino PEG (3400 MW, obtained from Shearwater Polymers, Huntsville, Ala.) in 250 ul of water was mixed with 0.1

Claim element	Patents in which element is found	Relevant Prior Art References										
percent	[8,535,705, c8]: The method of claim 1 wherein the solids concentration of the hydrogel ranges from 8.5% to 20% w/w.	<p>g of trifunctionally activated SC-PEG (5000 MW, also obtained from Shearwater Polymers) using syringe-to-syringe mixing. The reaction mixture was extruded onto a petri dish and formed a soft gel at room temperature. 0.15 gram of di-amino PEG in 250 µl of water was mixed with 0.1 g of tetrafunctionally activated SE-PEG (also from Shearwater Polymers) using syringe-to-syringe mixing. The reaction mixture was extruded onto a petri dish and formed a soft gel at room temperature. [50% solids in solution]</p> <div><p>TABLE 1</p><p><u>Preparation of Crosslinked Polymer Compositions</u></p><table><tr><th>Di-amino PEG</th><th>TSC-PEG + Aqueous Solvent</th></tr><tr><td>50 µl</td><td>0 mg + 50 µl water</td></tr><tr><td>50 µl</td><td>10 mg + 50 µl PBS</td></tr><tr><td>50 µl</td><td>10 mg + 100 µl PBS</td></tr><tr><td>250 µl</td><td>50 mg + 500 µl PBS</td></tr></table></div> <ul style="list-style-type: none">5,583,114: Table 1: [for example]: 50 mg/mL H₂O polylysine + 130 mg/mL PEG-SS2₃₄₀₀ ➔ ~8.25% solids	Di-amino PEG	TSC-PEG + Aqueous Solvent	50 µl	0 mg + 50 µl water	50 µl	10 mg + 50 µl PBS	50 µl	10 mg + 100 µl PBS	250 µl	50 mg + 500 µl PBS
Di-amino PEG	TSC-PEG + Aqueous Solvent											
50 µl	0 mg + 50 µl water											
50 µl	10 mg + 50 µl PBS											
50 µl	10 mg + 100 µl PBS											
250 µl	50 mg + 500 µl PBS											
Precursors further comprise PEG	[8,535,705, c15]: The method of claim 1 wherein at least one of the precursors is selected to further comprise a chemical group having the formula (CH ₂ CH ₂ O) _n .	<ul style="list-style-type: none">US 6,051,648 (Rhee): The first synthetic polymer is preferably a synthetic polypeptide or a polyethylene glycol that has been modified to contain multiple nucleophilic groups, such as primary amino (--NH₂) or thiol (--SH) groups.Gayet & Fortier: Teaches PEG component4,839,345: Proteins (nucleophiles) are water-soluble; PEG (electrophiles) is water soluble.5,328,955: Example 1 gives Collagen-PEG. Electrophilic polymer is also PEG-based:										

Claim element	Patents in which element is found	Relevant Prior Art References
		<p style="text-align: center;">FORMULA 1</p> <p>S-PEG: Difunctional PEG Succinimidyl Glutarate</p> <p style="text-align: center;">collagen-NH_2 collagen-NH_2</p> <p style="text-align: center;">$\text{collagen-HN-CO-(CH}_2)_3\text{-OC-O-PEG-O-CO-(CH}_2)_3\text{-CO-NH-collagen}$</p> <p><u>6,165,201</u>: Any monomer capable of being crosslinked to form a biocompatible surface coating may be used. The monomers may be small molecules, such as acrylic acid or vinyl caprolactam, larger molecules containing polymerizable groups, such as acrylate-capped polyethylene glycol (PEG-diacrylate),</p> <ul style="list-style-type: none">• <u>Sawhney et al., Macromolecules, (1993) 26, 581-587</u>: Macromers having a poly(ethylene glycol) central block, extended with oligomers of α-hydroxy acids such as oligo(dl-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation of cross-linked gels. These gels degrade upon hydrolysis of the oligo(α-hydroxy acid) regions into poly(ethylene glycol), the α-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular drug delivery.• <u>WO 2000/09087</u>: PEG succinimidyl succinates, PEG succinimidyl propionates, succinimidyl esters of amono acid or carboxymethylated PEG, and PEG succinamidyl succinamides are particularly suitable as electrophilically active macromers that react with nucleophilic group-containing macromers due to their high reactivity at physiological pH and speed of polymerization.• <u>WO 2000/033764</u>: FIG. 11 shows the variation in gelation time with the number

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>of amino groups for the reaction of 4 arm 10 kDa succinimidyl glutarate PEG ("SG-PEG") with di-, tri- or tetra-lysine.</p> <ul style="list-style-type: none">• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddlesFifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8. <p>$\text{PEG-COO-R-COO-NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG-COO-R-CONH-protein}$ <i>Two-Step</i></p> <p><i>PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional "double-ester" PEGs, as shown in Scheme 2.</p> <ul style="list-style-type: none">• <u>7,279,176</u>:<ol style="list-style-type: none">1. Synthesis of copolymer<p>1. Synthesis of copolymer</p><ol style="list-style-type: none">1. Synthesis of copolymer<ul style="list-style-type: none">• <u>WO 97/22371</u>: Hydrophilic polymers and, in particular, various polyethylene glycols, are preferred for use in the compositions ofthe present invention. As used herein, the term "PEG" refers to polymers having the repeating structure (OCH₂

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>CH₂)_n.</p> <ul style="list-style-type: none">• <u>6,371,975</u>: A biocompatible and biodegradable barrier material is applied to a tissue region, e.g., to seal a vascular puncture site. The barrier material comprises a compound, which is chemically cross-linked without use of an enzyme to form a non-liquid mechanical matrix. The compound preferably includes a protein comprising recombinant or natural serum albumin, which is mixed with a polymer that comprises poly(ethylene) glycol (PEG), and, most preferably, a multi-armed PEG polymer.• <u>Miranda</u>: The process of drying a complex mixture of macromolecules like PVP, PEG and agar showed an irreversible behavior upon hydration, probably as a function of physical crosslinking.• <u>Russell</u>: simple approach is described for preparing poly-(ethylene glycol) hydrogel materials with encapsulated seminaphthofluorescein (SNAFL)-organophosphorus hydrolase enzyme conjugates.
Nucleophilic and electrophilic groups crosslink to form a gel having an interior and an exterior	[7,009,034, c1]: the nucleophilic functional groups and electrophilic functional groups crosslink after contact with the tissue to form a hydrogel having an interior and an exterior, [7,332,566, c1]: and a biodegradable hydrogel, having an interior and an exterior, [7,332,566, c12]	<ul style="list-style-type: none">• <u>Gayet & Fortier</u>: [Col. 2 p. 178] “This ratio is the respective molar amount of activated hydroxyl groups of PEG versus free amino groups of BSA required to achieve polymerization of the hydrogel, taking into account that two activated hydroxyl groups are present on each molecule of PEG and 27 accessible free amino groups are available on each molecule of BSA.” <p>[Col. 2 p. 178] “when polymerization was achieved, the hydrogel film was cut into small pastilles (diameter 8 mm; thickness 1 or 1.5 mm)”</p> <p>[Col. 2 p. 178] “the hydrogel pastilles were then fully swollen and had reached their final shape and thickness”</p> <p>[pp. 178-179, bridging] “After loading, each pastille was mounted on a glass slide, and its edge covered with Liquid Paper ... in order to allow only one face to be available for diffusion in bulk medium”</p> <ul style="list-style-type: none">• <u>Prestwich</u>: p.7521, col. 2: The highly porous three-dimensional structures of the HA hydrogels suggest that they may be appropriate biodegradable scaffolds for

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>the adherence and growth of cells in three dimensions.</p> <p>p. 7519, Scheme 3: showing crosslinking:</p>  <p>p.7521, col. 2: The highly porous three-dimensional structures of the HA hydrogels suggest that they may be appropriate biodegradable scaffolds for the adherence and growth of cells in three dimensions.</p> <ul style="list-style-type: none">• <u>US 5,583,114</u>: The following procedure was used to prepare a two-component adhesive using a variety of protein sources, and bifunctional crosslinking agents. Aqueous solutions of a protein [<i>e.g.</i>, <i>poly-L-Lysine</i>] and a crosslinking agent [<i>i.e.</i>, <i>PEG-SS2</i> above] as listed in Table 1 were pipetted (0.2 ml of each solution) into a porcelain test well and mixed continuously with a stainless steel rod. The cure time and physical consistency of each of the two component adhesives are also listed in Table 1. <p>Col. 2 (Summary): The present invention is a nontoxic, absorbable adhesive sealant composition which may be used to bond and/or seal tissue.<u>Tse</u>:</p> <ul style="list-style-type: none">• <u>Tse</u>: The cyanoacrylate adhesives polymerize in the presence of anions, especially hydroxyl ions. This action means that it forms a firm adhesive bond when coming into contact with water or tissue moisture. The adhesive should be applied as a thin film over the prepared site.• <u>US 6,051,648 (Rhee)</u>: The present invention discloses a crosslinked polymer composition comprising a first synthetic polymer containing two or more nucleophilic groups, and a second synthetic polymer containing two or more electrophilic groups which are capable of covalently bonding to one another to form a three dimensional matrix. <p>for tissue augmentation, in the prevention of surgical adhesions, and for coating surfaces of synthetic implants, as drug delivery matrices and for ophthalmic applications.</p> <ul style="list-style-type: none">• <u>WO 00/09087</u>: Preferably the functionality of a macromer molecule is >1 so that a crosslinked network or hydrogel results upon polymerization. Hydrogels that

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>resorb or degrade over a period of time are preferred, and more preferably, those that resorb within one or a few months.</p> <p>Nucleophilic functional group-containing macromers optionally may be mixed with electrophilic group-containing macromers to rapidly initiate polymerization.</p> <p>In accordance with the present invention, methods are provided that permit diffuse coating of wide and complicated tissue geometries to form "regional" barriers, by coating essentially all tissues in the region of intervention with an adherent crosslinked hydrogel barrier.</p> <ul style="list-style-type: none">• <u>WO 2000/033764</u>: The biocompatible crosslinked polymers and their precursors described above may be used in a variety of applications, such as components of tissue adhesives, tissue sealants, drug delivery vehicles, wound covering agents, barriers in preventing postoperative adhesions, and others. These and other suitable applications are reviewed in Schlag and Redl, "Fibrin Sealant" in Operative Surgery, volumes 1-7 (1986) , which is incorporated herein by reference. <p>The biocompatible crosslinked polymers and their precursors described above may be used in a variety of applications, such as components of tissue adhesives, tissue sealants, drug delivery vehicles, wound covering agents, barriers in preventing postoperative adhesions, and others. These and other suitable applications are reviewed in Schlag and Redl, "Fibrin Sealant" in Operative Surgery, volumes 1-7 (1986) , which is incorporated herein by reference.</p> <ul style="list-style-type: none">• <u>US 5,614,587 (Rhee)</u>: Methods are disclosed for using the compositions to effect the attachment of a native tissue to the surface of another native tissue, a non-native tissue, or a synthetic implant.• <u>2014/0243428</u>: Therefore, the interfacial region toughened as a result of protonation of the carboxyl groups and subsequent increase in their hydrogen bonding. In contrast, the interior bulk regions remained soft because protons could not diffuse into the polymer network within the experimental timescales.• <u>4,839,345</u>: A₈ liquid was added to B₈ liquid, stirred and mixed at room temperature for 10 minutes, and the solution was poured into a polypropylene vessel of 200×250×2 mm of a thickness of 0.6 mm, and warmed for 2 minutes at

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>50° C.</p> <ul style="list-style-type: none">• <u>5,328,955</u>: The conjugates can be dehydrated to form a solid object. They grow to 5x or more when exposed to water.• <u>6,156,201</u>: Water-soluble coatings may form thin films, but more preferably form three-dimensional gels of controlled thickness.• <u>Champagne</u>: Clinically proven, the toxic degradation products of longer-chain cyanoacrylates are barely detectable on extraction studies, such that they are widely considered non-toxic ... the adhesive was generally sprayed on using a spray gun nozzle and pressurized nitrogen gas, which left a thin, uniform layer of polymer on the tissue surface that dried into a flexible sheet.• <u>Ellis & Shaikh</u>: Histoacryl ... enable[s] precise control of the quantity and the thickness of the adhesive film applied.• <u>Sawhney et al.</u>, these macromers form a cross-linked three-dimensional gel.• <u>WO 2000/09087</u>: Hydrogels are materials which absorb solvents (such as water) , undergo rapid swelling without discernible dissolution, and maintain three-dimensional networks capable of reversible deformation.• <u>Zhao</u>: Hydrogels are generally considered as biocompatible materials because of their high water content. They have been used in a variety of biomaterial and biotechnology applications, such as tissue engineering, artificial organs, and drug delivery.• <u>Davis</u>: Teaches “medical version of super glue” which inherently has interior and exterior and coats surface of substrate.• <u>7,279,176</u>: Hydrogels releasing or producing NO, most preferably photopolymerizable biodegradable hydrogels capable of releasing physiological amounts of NO for prolonged periods of time, are applied to sites on or in a patient in need of treatment thereof for disorders such as restenosis, thrombosis, asthma, wound healing, arthritis, penile erectile dysfunction or other conditions where NO plays a significant role.• <u>6,162,241</u>: A method of controlling hemostasis by applying a hemostatic agent in a tissue sealant composition. The tissue sealant is a biodegradable, biocompatible synthetic polymer that may not intrinsically possess strong hemostatic properties.• <u>WO 97/22371</u>: We have found that the preferred compositions of the invention

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>tend to have unusually high tackiness, making them particularly suitable for use as bioadhesives, for example, for use in surgery.</p> <ul style="list-style-type: none">• <u>Miranda</u>: The process of drying a complex mixture of macromolecules like PVP, PEG and agar showed an irreversible behavior upon hydration, probably as a function of physical crosslinking.
Exterior has a substrate coating surface	<p>[7,009,034, c1]: with the exterior having at least one substrate coating surface and</p> <p>[7,332,566, c1]: with the exterior having a substrate coating surface,</p> <p>[7,332,566, c8]: The polymeric coating of claim 1 wherein the biodegradable hydrogel is adherent to the substrate.</p> <p>[7,332,566, c12]: with the exterior having at least one tissue substrate coating surface</p>	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: The present invention discloses a crosslinked polymer composition comprising a first synthetic polymer containing two or more nucleophilic groups, and a second synthetic polymer containing two or more electrophilic groups which are capable of covalently bonding to one another to form a three dimensional matrix. <p>for tissue augmentation, in the prevention of surgical adhesions, and for coating surfaces of synthetic implants, as drug delivery matrices and for ophthalmic applications.</p> <ul style="list-style-type: none">• <u>US 5,614,587 (Rhee)</u>: In a particularly preferred method for effecting the attachment of a first surface to a second surface, nonfibrillar collagen and a multifunctionally activated synthetic hydrophilic polymer are mixed to initiate crosslinking...• <u>WO 00/09087</u>: In accordance with the present invention, methods are provided that permit diffuse coating of wide and complicated tissue geometries to form "regional" barriers, by coating essentially all tissues in the region of intervention with an adherent crosslinked hydrogel barrier.• <u>Tse</u>: Butyl-2-cyanoacrylate tissue adhesive successfully sealed three cases of CSF leaks encountered during orbital surgery. The application of tissue adhesive was followed by prompt cessation of the leak.• <u>Gayet & Fortier</u>: We believe that this family of BSA-PEG hydrogels could be useful for the preparation of controlled release devices in the field of wound dressing.• <u>Prestwich</u>: p.7521, col. 2: The highly porous three-dimensional structures of the HA hydrogels suggest that they may be appropriate biodegradable scaffolds for the adherence and growth of cells in three dimensions.• <u>2014/0243428</u>: In a certain embodiment, the disclosure provides for a self-healing coating or a self-healing sealant comprising a hydrogel of the disclosure.

Claim element	Patents in which element is found	Relevant Prior Art References
		<ul style="list-style-type: none">• <u>4,839,345</u>: The present invention is directed to a hydrated adhesive gel...• <u>5,328,955</u>: The conjugates and compositions containing the conjugates can be coated on to various medical devices, including catheters, bone implants, and platinum wires to treat aneurysms.• <u>6,156,201</u>: it is an object of the present invention to provide apparatus and methods that enable a tissue coating comprising two or more crosslinkable fluids to be applied in situ as a spray.• <u>Champagne</u>: Clinically proven, the toxic degradation products of longer-chain cyanoacrylates are barely detectable on extraction studies, such that they are widely considered non-toxic ... the adhesive was generally sprayed on using a spray gun nozzle and pressurized nitrogen gas, which left a thin, uniform layer of polymer on the tissue surface that dried into a flexible sheet.• <u>Ellis & Shaikh</u>: Histoacryl ... enable[s] precise control of the quantity and the thickness of the adhesive film applied ... we think histoacryl glue is the ideal tissue adhesive for surface cutaneous wound closures... our experience with tissue adhesives indicate the use of fibrin glue mainly on the undersurface of flaps.• <u>Pathak, J.A.C.S. 1992, 114, 8311-8312</u>: The viability of the encapsulated cells was measured by trypan blue exclusion assay (Sigma). Human foreskin fibroblasts (HFF), Chinese hamster ovary cells (CHO-K1), and /3 cell insuloma cells (RiN5F)IS were found to be viable (more than 95%) after encapsulation.• <u>Sawhney et al., Macromolecules, (1993) 26, 581-587</u>: Macromers having a poly(ethylene glycol) central block, extended with oligomers of a-hydroxy acids such as oligo(dl-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation of cross-linked gels. These gels degrade upon hydrolysis of the oligo(a-hydroxy acid) regions into poly(ethylene glycol), the a-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>drug delivery.</p> <ul style="list-style-type: none">• <u>WO 2000/09087</u>: In a preferred method, a crosslinked regional barrier is formed in situ, for example, by free radical polymerization initiated by a redox system or thermal initiation, wherein two components of an initiating system are simultaneously, sequentially or separately instilled in a body cavity to obtain widespread dispersal and coating of all or most visceral organs within that cavity prior to gelation and crosslinking of the regional barrier.• <u>WO 2000/033764</u>: Biocompatible crosslinked polymers, and methods for their preparation and use, are disclosed in which the biocompatible crosslinked polymers are formed from water soluble precursors having electrophilic and nucleophilic groups capable of reacting and crosslinking in situ. Methods for making the resulting biocompatible crosslinked polymers biodegradable or not are provided, as are methods for controlling the rate of degradation. The crosslinking reactions may be carried out in situ on organs or tissues or outside the body. Applications for such biocompatible crosslinked polymers and their precursors include controlled delivery of drugs, prevention of post-operative adhesions, coating of medical devices such as vascular grafts, wound dressings and surgical sealants.• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>Zhao</u>: Hydrogels are generally considered as biocompatible materials because of their high water content. They have been used in a variety of biomaterial and biotechnology applications, such as tissue engineering, artificial organs, and drug delivery.• <u>Davis</u>: Teaches "medical version of super glue" which inherently has interior and exterior and coats surface of substrate.• <u>7,279,176</u>: Hydrogels releasing or producing NO, most preferably photopolymerizable biodegradable hydrogels capable of releasing physiological amounts of NO for prolonged periods of time, are applied to sites on or in a

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>patient in need of treatment thereof for disorders such as restenosis, thrombosis, asthma, wound healing, arthritis, penile erectile dysfunction or other conditions where NO plays a significant role. The polymeric materials can also be formed into films, coatings, or microparticles.</p> <ul style="list-style-type: none">• <u>6,162,241</u>: A method of controlling hemostasis by applying a hemostatic agent in a tissue sealant composition. The tissue sealant is a biodegradable, biocompatible synthetic polymer that may not intrinsically possess strong hemostatic properties.• <u>WO 97/22371</u>: We have found that the preferred compositions of the invention tend to have unusually high tackiness, making them particularly suitable for use as bioadhesives, for example, for use in surgery.•
A visualization agent	[7,009,034, c1]: and a visualization agent such that [7,332,566, c1]: a biocompatible visualization agent,	<ul style="list-style-type: none">• <u>Gayet & Fortier</u>: [p. 180, Table 2] Methylene Blue listed as a ‘drug’• <u>Tse</u>: p. 1337 col. 3: “There is a color additive in the tissue adhesive, which facilitates visualization and assessment of plaque thickness.”• <u>US 5,583,114</u>: Col. 1 (background): For example, cyanoacrylate adhesives such as Histoacryl® adhesive available from B. Braun, Melsungen, Germany or Vetbond tissue adhesive available from 3M, St. Paul., Minn. May be used to bond tissue.• <u>US 6,051,648 (Rhee)</u>: The crosslinked polymer compositions can also be prepared to contain various imaging agents such as iodine or barium sulfate, or fluorine, in order to aid visualization of the compositions after administration via X-ray, or 19 F-MRI, respectively ... Because it is opaque and less tacky than nonfibrillar collagen, fibrillar collagen is less preferred for use in bioadhesive compositions.• <u>WO 2000/033764</u>: Where convenient, the biocompatible crosslinked polymer or precursor solutions (or both) may contain visualization agents to improve their visibility during surgical procedures. Visualization agents are especially useful when used in MIS procedures, due among other reasons to their improved visibility on a color monitor. Visualization agents may be selected from among any of the various non-toxic colored substances suitable for use in medical implantable medical devices, such as FD&C dyes 3 and 6, eosin, methylene blue, indocyanine green, or colored dyes normally found in synthetic surgical sutures. The preferred color is green or blue because it has better visibility in presence of

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>blood or on a pink or white tissue background. Red is the least preferred color.</p> <p>The visualization agent may be present in either a crosslinker or functional polymer solution, preferably in a functional polymer solution. The preferred colored substance may or may not become incorporated into the biocompatible crosslinked polymer. Preferably, however, the visualization agent does not have a functional group capable of reacting with the crosslinker or functional polymer. The visualization agent may be used in small quantities, preferably less than 1% weight/volume, more preferably less than 0.01% weight/volume and most preferably less than 0.001% weight/volume concentration. Additional visualization agents may be used, such as fluorescent (e.g., green or yellow fluorescent under visible light) compounds (e.g., fluorescein or eosin), x-ray contrast agents (e.g., iodinated compounds) for visibility under x-ray imaging equipment, ultrasonic contrast agents, or MRI contrast agents (e.g., Gadolinium containing compounds)</p> <ul style="list-style-type: none">• <u>Tse</u>: There is a color additive in the tissue adhesive, which facilitates visualization and assessment of plaque thickness• <u>2014/0243428</u>: The coating was colored using a dye for easy visualization and the observed color change after healing is caused by its exposure to low-pH buffer.• <u>5,719,031</u>: This invention relates to polymers labeled with a borapolyaza-s-indacene fluorescent dye to the point that significant fluorescence quenching occurs, such that degradation of the polymer results in fluorescence enhancement.• <u>6,156,201</u>: If desired, one or both crosslinkable solutions may contain dyes or other means for visualizing the hydrogel coating.• <u>CA 1054517</u>: In the practice of the present invention the primary-amine-containing polymeric backbone is allowed to react with the fluorescent dye which has been functionalized so as to enable it to react covalently with the repeating functional groups of the polymeric material• <u>WO 95/34605</u>: This invention is directed, in part, to a method for the manufacture of tinted hydrogel materials using a vat dye wherein the tinting and polymerization process take place in a single reaction medium thereby

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		<p>simplifying the overall tinting process.</p> <ul style="list-style-type: none">• <u>Bryant et al</u>: The glycosaminoglycan (GAG) content was determined using the dimethylmethylene blue dye method• <u>Champagne</u>: Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient’s tissue.• <u>WO 2000/033764</u>: Where convenient, the biocompatible crosslinked polymer or precursor solutions (or both) may contain visualization agents to improve their visibility during surgical procedures. Visualization agents are especially useful when used in MIS procedures, due among other reasons to their improved visibility on a color monitor. Visualization agents may be selected from among any of the various non-toxic colored substances suitable for use in medical implantable medical devices, such as FD&C dyes 3 and 6, eosin, methylene blue, indocyanine green, or colored dyes normally found in synthetic surgical sutures. The preferred color is green or blue because it has better visibility in presence of blood or on a pink or white tissue background. Red is the least preferred color. The visualization agent may be present in either a crosslinker or functional polymer solution, preferably in a functional polymer solution. The preferred colored substance may or may not become incorporated into the biocompatible crosslinked polymer. Preferably, however, the visualization agent does not have a functional group capable of reacting with the crosslinker or functional polymer. The visualization agent may be used in small quantities, preferably less than 1% weight/volume, more preferably less than 0.01% weight/volume and most preferably less than 0.001% weight/volume concentration.• <u>US 5,292,362</u>: The composition of the present invention may also include indigenous or exogenous chromophores to facilitate visualization of the material during placement into warm blooded animals. Use of a chromophore will allow material which becomes displaced from the desired application site to be easily visualized, and subsequently removed using a cellulose sponge, gauze pad, or

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>other absorbing material ... Chromophores that may be used, include, but are not limited to fluorescein isothiocyanate, indocyanine green, silver compounds such as silver nitrate, rose bengal, nile blue and Evans Blue, Q-Switch™, a dye made by Kodak, Inc., Sudan III, Sudan Black B and India Ink. The chromophores are preferably present in a concentration of from about 0.01 to 50% by weight based on the total weight of the composition. Other chromophores as would be obvious to one skilled in the art may also be employed.</p> <ul style="list-style-type: none">• <u>Zhao</u>: StudiessRelease of model drugs from the hydrogels was studied. The first type of model drug was an m-PEG-dye, which was synthesized in our laboratory. The m-PEG-dyes were loaded into the one-step hydrogels by a diffusion process, whereas the two-step hydrogels formed in the presence of m-PEG-dye ... the FITC-BSA was used as a protein model in a drug release study.• <u>Davis</u>: One product widely used in A&E departments contains a non-toxic blue dye which enables visualisation of the quantity applied. Surgical glue may be used as an alternative, or adjunct to more traditional methods of wound closure, such as sutures, staples, and wound closure ships• <u>7,279,176</u>: Useful photoinitiators are those which can be used to initiate by free radical generation polymerization of the macromers without cytotoxicity and within a short time frame, minutes at most and most preferably seconds. Preferred dyes as initiators of choice for LWUV initiation are ethyl eosin, 2,2-dimethoxy-2-phenyl acetophenone, other acetophenone derivatives, and camphorquinone. There are several photooxidizable and photoreducible dyes that may be used to initiate polymerization. These include acridine dyes, for example, acriblarine; thiazine dyes, for example, thionine; xanthine dyes, for example, rose bengal; and phenazine dyes, for example, methylene blue.• <u>6,162,241</u>: Useful photoinitiators are those which can be used to initiate by free radical generation polymerization of the macromers without cytotoxicity and within a short time frame, minutes at most and most preferably seconds. Preferred dyes as initiators of choice for LWUV initiation are ethyl eosin, 2,2-dimethoxy-2-phenyl acetophenone, other acetophenone derivatives, and camphorquinone. In all cases, crosslinking and polymerization are initiated among copolymers by a light-activated free-radical polymerization initiator such

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		<p>as 2,2-dimethoxy-2-phenylacetophenone or a combination of ethyl eosin and triethanolamine, for example.</p> <ul style="list-style-type: none">• <u>WO 97/22371</u>: The crosslinked polymer compositions can also be prepared to contain various imaging agents such as iodine or barium sulfate, or fluorine, in order to aid visualization of the compositions after administration via X-ray, or ¹ F-MRI, respectively.
Visulaization agent is: FD&C Blue #1, FD&C Blue #2, methylene blue, indocyanine green, visualization agents that provide a blue color, and visualization agents that provide a green color.	<p>[7,009,034, c6]: The polymeric coating method of claim 1, wherein the visualization agent is chosen from the group consisting of FD&C Blue #1, FD&C Blue #2, methylene blue, indocyanine green, visualization agents that provide a blue color, and visualization agents that provide a green color.</p> <p>[7,332,566, c3]: The polymeric coating of claim 1 wherein the visualization agent is chosen from the group consisting of FD&C Blue #1, FD&C Blue #2, methylene blue, indocyanine green, visualization agents that provide a blue color, and visualization agents that provide a green color.</p> <p>[7,332,566, c15]</p> <p>[7,332,566, c27]</p> <p>[7,592,418, c4]</p>	<ul style="list-style-type: none">• Tse: Histoacryl blue is colored with D&C violet #2 [<i>via Package Insert</i>].• <u>Gayet & Fortier</u>: [p. 180, Table 2] Methylene Blue listed as a ‘drug’• <u>WO 95/34605</u>: Example 5 The procedure of Example 1 is repeated except that the composition comprising the monomer, the cross-linking agent and the leuco sulfate ester of Vat Green No. 1 dye further comprises about 38 weight percent water. The polymeric material was then released from the molds and hydrated in buffered saline to provide a tinted hydrogel material in the form of contact lenses having a blue coloration which coloration is resistant to autoclaving and which material contains about 38 weight percent water.• <u>Bryant et al</u>: The glycosaminoglycan (GAG) content was determined using the dimethylmethylene blue dye method• <u>Champagne</u>: Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient’s tissue.• <u>Histoacryl Blue Package Insert</u>: Histoacryl® Blue is colored with the dye D&C Violet #2• <u>Ellis</u>: 2-cyanoacrylate mixed with an FDA-approved dye for easy visibility.• <u>Pathak</u>: The viability of the encapsulated cells was measured by trypan blue exclusion assay (Sigma).• <u>WO 2000/033764</u>: Where convenient, the biocompatible crosslinked polymer or precursor solutions (or both) may contain visualization agents to improve their visibility during surgical procedures. Visualization agents are especially useful when used in MIS procedures, due among other reasons to their improved

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		<p>visibility on a color monitor. Visualization agents may be selected from among any of the various non-toxic colored substances suitable for use in medical implantable medical devices, such as FD&C dyes 3 and 6, eosin, methylene blue, indocyanine green, or colored dyes normally found in synthetic surgical sutures. The preferred color is green or blue because it has better visibility in presence of blood or on a pink or white tissue background. Red is the least preferred color. The visualization agent may be present in either a crosslinker or functional polymer solution, preferably in a functional polymer solution. The preferred colored substance may or may not become incorporated into the biocompatible crosslinked polymer. Preferably, however, the visualization agent does not have a functional group capable of reacting with the crosslinker or functional polymer. The visualization agent may be used in small quantities, preferably less than 1% weight/volume, more preferably less than 0.01% weight/volume and most preferably less than 0.001% weight/volume concentration.</p> <ul style="list-style-type: none">• <u>US 5,292,362</u>: The composition of the present invention may also include indogenous or exogenous chromophores to facilitate visualization of the material during placement into warm blooded animals. Use of a chromophore will allow material which becomes displaced from the desired application site to be easily visualized, and subsequently removed using a cellulose sponge, gauze pad, or other absorbing material ... Chromophores that may be used, include, but are not limited to fluorescein isothiocyanate, indocyanine green, silver compounds such as silver nitrate, rose bengal, nile blue and Evans Blue, Q-Switch™, a dye made by Kodak, Inc., Sudan III, Sudan Black B and India Ink. The chromophores are preferably present in a concentration of from about 0.01 to 50% by weight based on the total weight of the composition. Other chromophores as would be obvious to one skilled in the art may also be employed.• <u>Davis</u>: One product widely used in A&E departments contains a non-toxic blue dye which enables visualisation of the quantity applied. Surgical glue may be used as an alternative, or adjunct to more traditional methods of wound closure, such as sutures, staples, and wound closure ships. [<i>Histoacryl® Blue is colored with the dye D&C Violet #2</i>]• <u>7,279,176</u>: Useful photoinitiators are those which can be used to initiate by free

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		<p>radical generation polymerization of the macromers without cytotoxicity and within a short time frame, minutes at most and most preferably seconds. Preferred dyes as initiators of choice for LWUV initiation are ethyl eosin, 2,2-dimethoxy-2-phenyl acetophenone, other acetophenone derivatives, and camphorquinone. There are several photooxidizable and photoreducible dyes that may be used to initiate polymerization. These include acridine dyes, for example, acriblarine; thiazine dyes, for example, thionine; xanthine dyes, for example, rose bengal; and phenazine dyes, for example, methylene blue.</p> <ul style="list-style-type: none">• <u>6,162,241</u>: Useful photoinitiators are those which can be used to initiate by free radical generation polymerization of the macromers without cytotoxicity and within a short time frame, minutes at most and most preferably seconds. Preferred dyes as initiators of choice for LWUV initiation are ethyl eosin, 2,2-dimethoxy-2-phenyl acetophenone, other acetophenone derivatives, and camphorquinone. In all cases, crosslinking and polymerization are initiated among copolymers by a light-activated free-radical polymerization initiator such as 2,2-dimethoxy-2-phenylacetophenone or a combination of ethyl eosin and triethanolamine, for example.• <u>Russell</u>: simple approach is described for preparing poly-(ethylene glycol) hydrogel materials with encapsulated seminaphthofluorescein (SNAFL)-organophosphorus hydrolase enzyme conjugates.
Visualization agent dispersed within the hydrogel that emits light detectable to human eye to enable visualization of coating	<p>[7,009,034, c1]: the visualization agent being at least partially disposed within the interior and reflecting or emitting light at a wavelength detectable to a human eye to thereby provide a means for visualization of the coating by a human eye.</p> <p>[7,332,566, c1]: and the visualization agent being at least partially disposed within the interior,</p> <p>[7,332,566, c12]: and the visualization agent being at least partially disposed within the interior,</p>	<ul style="list-style-type: none">• <u>Gayete</u>: [Col. 2 p. 178] “Drug solutions (i.e., methylene blue) were made at 250 µg/mL ... in PBS buffer pH 7.6 in which pastilles of hydrogel were allowed to load during 24 h at room temperature” <p>[Col. 1 p. 179] “The bulk medium was continuously pumped into the flow cells of a 8452A Hewlett Packard spectrophotometer to monitor the release of the drug at its maximum absorption wavelength.”</p> <ul style="list-style-type: none">• <u>US 5,583,114</u>: Col. 1 (background): For example, cyanoacrylate adhesives such as Histoacryl® adhesive available from B. Braun, Melsungen, Germany or Vetbond tissue adhesive available from 3M, St. Paul., Minn. May be used to bond tissue.• <u>Tse</u>: p. 1337 col. 3: “There is a color additive in the tissue adhesive, which

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>facilitates visualization and assessment of plaque thickness.”</p> <ul style="list-style-type: none">• <u>US 6,051,648</u>: The crosslinked polymer compositions can also be prepared to contain various imaging agents such as iodine or barium sulfate, or fluorine, in order to aid visualization of the compositions after administration via X-ray, or 19 F-MRI, respectively.• <u>WO 2000/033764</u>: Where convenient, the biocompatible crosslinked polymer or precursor solutions (or both) may contain visualization agents to improve their visibility during surgical procedures. Visualization agents are especially useful when used in MIS procedures, due among other reasons to their improved visibility on a color monitor. Visualization agents may be selected from among any of the various non-toxic colored substances suitable for use in medical implantable medical devices, such as FD&C dyes 3 and 6, eosin, methylene blue, indocyanine green, or colored dyes normally found in synthetic surgical sutures. The preferred color is green or blue because it has better visibility in presence of blood or on a pink or white tissue background. Red is the least preferred color. <p>The visualization agent may be present in either a crosslinker or functional polymer solution, preferably in a functional polymer solution. The preferred colored substance may or may not become incorporated into the biocompatible crosslinked polymer. Preferably, however, the visualization agent does not have a functional group capable of reacting with the crosslinker or functional polymer. The visualization agent may be used in small quantities, preferably less than 1% weight/volume, more preferably less than 0.01% weight/volume and most preferably less than 0.001% weight/volume concentration. Additional visualization agents may be used, such as fluorescent (e.g., green or yellow fluorescent under visible light) compounds (e.g., fluorescein or eosin), x-ray contrast agents (e.g., iodinated compounds) for visibility under x-ray imaging equipment, ultrasonic contrast agents, or MRI contrast agents (e.g., Gadolinium containing compounds) .</p> <ul style="list-style-type: none">• <u>2014/0243428</u>: The coating was colored using a dye for easy visualization and the

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		<p>observed color change after healing is caused by its exposure to low-pH buffer.</p> <ul style="list-style-type: none">• <u>5,719,031</u>: This invention relates to polymers labeled with a borapolyaza-s-indacene fluorescent dye to the point that significant fluorescence quenching occurs, such that degradation of the polymer results in fluorescence enhancement• <u>WO 95/34605</u>: Example 5 The procedure of Example 1 is repeated except that the composition comprising the monomer, the cross-linking agent and the leuco sulfate ester of Vat Green No. 1 dye further comprises about 38 weight percent water. The polymeric material was then released from the molds and hydrated in buffered saline to provide a tinted hydrogel material in the form of contact lenses having a blue coloration which coloration is resistant to autoclaving and which material contains about 38 weight percent water.• <u>Champagne</u>: Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient's tissue.• <u>Pathak</u>: The viability of the encapsulated cells was measured by trypan blue exclusion assay (Sigma).• <u>WO 2000/033764</u>: Where convenient, the biocompatible crosslinked polymer or precursor solutions (or both) may contain visualization agents to improve their visibility during surgical procedures. Visualization agents are especially useful when used in MIS procedures, due among other reasons to their improved visibility on a color monitor. Visualization agents may be selected from among any of the various non-toxic colored substances suitable for use in medical implantable medical devices, such as FD&C dyes 3 and 6, eosin, methylene blue, indocyanine green, or colored dyes normally found in synthetic surgical sutures. The preferred color is green or blue because it has better visibility in presence of blood or on a pink or white tissue background. Red is the least preferred color.• The visualization agent may be present in either a crosslinker or functional polymer solution, preferably in a functional polymer solution. The preferred

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		<p>colored substance may or may not become incorporated into the biocompatible crosslinked polymer. Preferably, however, the visualization agent does not have a functional group capable of reacting with the crosslinker or functional polymer. The visualization agent may be used in small quantities, preferably less than 1% weight/volume, more preferably less than 0.01% weight/volume and most preferably less than 0.001% weight/volume concentration.</p> <ul style="list-style-type: none">• <u>US 5,292,362</u>: The composition of the present invention may also include indogenous or exogenous chromophores to facilitate visualization of the material during placement into warm blooded animals. Use of a chromophore will allow material which becomes displaced from the desired application site to be easily visualized, and subsequently removed using a cellulose sponge, gauze pad, or other absorbing material ... Chromophores that may be used, include, but are not limited to fluorescein isothiocyanate, indocyanine green, silver compounds such as silver nitrate, rose bengal, nile blue and Evans Blue, Q-Switch™, a dye made by Kodak, Inc., Sudan III, Sudan Black B and India Ink. The chromophores are preferably present in a concentration of from about 0.01 to 50% by weight based on the total weight of the composition. Other chromophores as would be obvious to one skilled in the art may also be employed.• <u>Davis</u>: One product widely used in A&E departments contains a non-toxic blue dye which enables visualisation of the quantity applied. Surgical glue may be used as an alternative, or adjunct to more traditional methods of wound closure, such as sutures, staples, and wound closure ships. [<i>Histoacryl® Blue is colored with the dye D&C Violet #2</i>]• <u>7,279,176</u>: Useful photoinitiators are those which can be used to initiate by free radical generation polymerization of the macromers without cytotoxicity and within a short time frame, minutes at most and most preferably seconds. Preferred dyes as initiators of choice for LWUV initiation are ethyl eosin, 2,2-dimethoxy-2-phenyl acetophenone, other acetophenone derivatives, and camphorquinone. There are several photooxidizable and photoreducible dyes that may be used to initiate polymerization. These include acridine dyes, for example, acriblarine; thiazine dyes, for example, thionine; xanthine dyes, for example, rose bengal; and phenazine dyes, for example, methylene blue.

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		<ul style="list-style-type: none">• <u>6,162,241</u>: Useful photoinitiators are those which can be used to initiate by free radical generation polymerization of the macromers without cytotoxicity and within a short time frame, minutes at most and most preferably seconds. Preferred dyes as initiators of choice for LWUV initiation are ethyl eosin, 2,2-dimethoxy-2-phenyl acetophenone, other acetophenone derivatives, and camphorquinone. In all cases, crosslinking and polymerization are initiated among copolymers by a light-activated free-radical polymerization initiator such as 2,2-dimethoxy-2-phenylacetophenone or a combination of ethyl eosin and triethanolamine, for example.• <u>Russell</u>: simple approach is described for preparing poly-(ethylene glycol) hydrogel materials with encapsulated seminaphthofluorescein (SNAFL)-organophosphorus hydrolase enzyme conjugates.•
Concentration of visualization agent at least 0.1 mg/mL	[7,332,566, c12]: and at least about 0.1 mg/ml of an unbleached visualization agent	<ul style="list-style-type: none">• <u>Gayete</u>: [Col. 2 p. 178] “Drug solutions (i.e., methylene blue) were made at 250 µg/mL ... in PBS buffer pH 7.6 in which pastilles of hydrogel were allowed to load during 24 h at room temperature”• <u>WO 95/34605</u>: Example 2 A solution of <u>0.1 weight percent</u> of the leuco sulfate ester of Vat Blue #6 dye was made up in hydroxyethyl methacrylate containing 0.5 weight percent ethylene glycol dimethacrylate as a cross-linking agent.• <u>WO 2000/033764</u>: Where convenient, the biocompatible crosslinked polymer or precursor solutions (or both) may contain visualization agents to improve their visibility during surgical procedures. Visualization agents are especially useful when used in MIS procedures, due among other reasons to their improved visibility on a color monitor. Visualization agents may be selected from among any of the various non-toxic colored substances suitable for use in medical implantable medical devices, such as FD&C dyes 3 and 6, eosin, methylene blue, indocyanine green, or colored dyes normally found in synthetic surgical sutures. The preferred color is green or blue because it has better visibility in presence of blood or on a pink or white tissue background. Red is the least preferred color. The visualization agent may be present in either a crosslinker or functional polymer solution, preferably in a functional polymer solution. The preferred colored substance may or may not become incorporated into the biocompatible

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>crosslinked polymer. Preferably, however, the visualization agent does not have a functional group capable of reacting with the crosslinker or functional polymer. The visualization agent may be used in small quantities, preferably less than 1% weight/volume, more preferably less than 0.01% weight/volume and most preferably less than 0.001% weight/volume concentration.</p> <ul style="list-style-type: none">• <u>US 5,292,362</u>: The composition of the present invention may also include indigenous or exogenous chromophores to facilitate visualization of the material during placement into warm blooded animals. Use of a chromophore will allow material which becomes displaced from the desired application site to be easily visualized, and subsequently removed using a cellulose sponge, gauze pad, or other absorbing material ... Chromophores that may be used, include, but are not limited to fluorescein isothiocyanate, indocyanine green, silver compounds such as silver nitrate, rose bengal, nile blue and Evans Blue, Q-Switch™, a dye made by Kodak, Inc., Sudan III, Sudan Black B and India Ink. The chromophores are preferably present in a concentration of from about 0.01 to 50% by weight based on the total weight of the composition. Other chromophores as would be obvious to one skilled in the art may also be employed.
Visualization agent causes a visually observable change that indicates that hydrogel has reached a predetermined thickness	<p>[7,009,034, c16]: the visualization agent causes a visually observable change that indicates that a crosslinked hydrogel having a predetermined thickness has been formed on the tissue of a patient</p> <p>[7,332,566, c1]: wherein the visualization agent has a predetermined concentration that indicates a predetermined thickness of the hydrogel as deposited on the substrate</p> <p>[7,332,566, c12]: wherein the visualization agent has a predetermined concentration that indicates a predetermined thickness of the hydrogel as deposited on substrate.</p> <p>[7,592,418]: selecting a concentration of visualization agent for the polymer composition so that when the hydrogel is applied onto a substrate to reach an average predetermined thickness of the hydrogel, an observable change occurs indicating the predetermined thickness of hydrogel has been deposited on the</p>	<ul style="list-style-type: none">• <u>US 5,583,114</u>: Col. 1 (background): For example, cyanoacrylate adhesives such as Histoacryl® adhesive available from B. Braun, Melsungen, Germany or Vetbond tissue adhesive available from 3M, St. Paul., Minn. May be used to bond tissue.• <u>Tse</u>: Fig. 1 caption, p. 1338: “Faint gray-blue tint indicates adequate thickness of adhesive film.”• <u>Champagne</u>: Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient’s tissue.

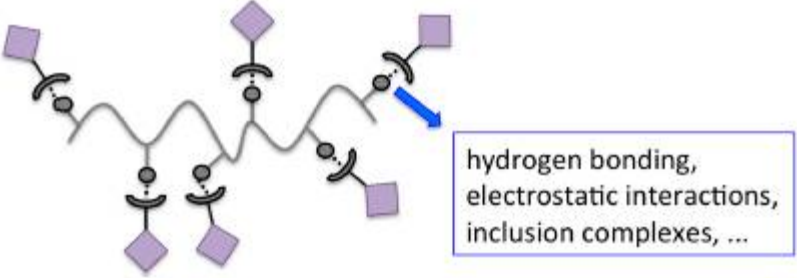
Claim element	Patents in which element is found	Relevant Prior Art References
Observable change is not being able to see through the polymer composition	<p>substrate</p> <p>[7,009,034, c18]: The method of claim 16, wherein the observable change is not being able to see a substrate through the polymer composition.</p> <p>[7,332,566, c11]: The polymeric coating of claim 1 wherein the predetermined thickness of the hydrogel is indicated by an observable change of not being able to see the substrate tissue through the polymer composition, not being able to see patterns in the substrate tissue surface through the polymer composition, the features of the substrate are obscured, or not being able to see the microvasculature on the substrate tissue.</p> <p>[7,332,566, c25]</p>	<ul style="list-style-type: none"> • <u>Tse</u>: p. 1337 col. 3: “There is a color additive in the tissue adhesive, which facilitates visualization and assessment of plaque thickness.” • <u>Champagne</u>: Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient’s tissue.
<p>Observable change is not being able to see patterns in substrate surface through the polymer composition</p> <p>Observable change is not being able to see through the polymer composition</p>	<p>[7,009,034, c19]: The method of claim 16, wherein the observable change is not being able to see patterns in a substrate surface through the polymer composition.</p> <p>[7,332,566, c11]: The polymeric coating of claim 1 wherein the predetermined thickness of the hydrogel is indicated by an observable change of not being able to see the substrate tissue through the polymer composition, not being able to see patterns in the substrate tissue surface through the polymer composition, the features of the substrate are obscured, or not being able to see the microvasculature on the substrate tissue.</p> <p>[7,332,566, c22]</p> <p>[7,592,418, c11] The method of claim 1 wherein the observable change is not being able to see the substrate tissue through the polymer composition, not being able to see patterns in the substrate surface through the polymer composition, the features of the substrate are obscured, or not being able to see the microvasculature on the substrate tissue.</p> <p>[7,592,418, c13]: The method of claim 11 wherein the observable change is not being able to see through the polymer composition.</p>	<ul style="list-style-type: none"> • <u>Tse</u>: p. 1337 col. 3: “There is a color additive in the tissue adhesive, which facilitates visualization and assessment of plaque thickness.” • <u>Champagne</u>: Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient’s tissue.

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	<p>[7,592,418, c14]: The method of claim 11 wherein the observable change is not being able to see patterns in the substrate surface through the polymer composition.</p> <p>[7,592,418, c15]: The method of claim 11 wherein the observable change is that the features of the substrate are obscured.</p> <p>[7,592,418, c16]: The method of claim 11 wherein the observable change is not being able to see the microvasculature on the substrate tissue.</p>	
Mixing visualization agent at a selected concentration with reactive precursor species	<p>[7,009,034, c20]: The method of claim 16, further comprising mixing the visualization agent at a selected concentration with reactive precursor species.</p> <p>[7,332,566, c1]: wherein the visualization agent has a predetermined concentration that indicates a predetermined thickness of the hydrogel as deposited on the substrate</p> <p>[7,332,566, c25]: selecting a concentration of visualization agent for the polymer composition that results in a visually observable change when the polymer composition is applied to a substrate tissue at a predetermined thickness</p>	<ul style="list-style-type: none"> • <u>Tse</u>: p. 1337 col. 3: “There is a color additive in the tissue adhesive, which facilitates visualization and assessment of plaque thickness.” • <u>Champagne</u>: Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient’s tissue.
Color of the hydrogel indicates the predetermined thickness	<p>[7,009,034, c13]: The method of claim 1, further comprising: applying the hydrogel onto the tissue until an average thickness is reached in which the color of the hydrogel indicates that a predetermined thickness of hydrogel has been deposited on the tissue.</p> <p>[7,332,566, c25]: selecting a concentration of visualization agent for the polymer composition that results in a visually observable change when the polymer composition is applied to a substrate tissue at a predetermined thickness</p>	<ul style="list-style-type: none"> • <u>US 5,583,114</u>: Col. 1 (background): For example, cyanoacrylate adhesives such as Histoacryl® adhesive available from B. Braun, Melsungen, Germany or Vetbond tissue adhesive available from 3M, St. Paul., Minn. May be used to bond tissue. • <u>Tse</u>: Fig. 1 caption, p. 1338: “Faint gray-blue tint indicates adequate thickness of adhesive film.” • <u>Champagne</u>: Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient’s tissue.

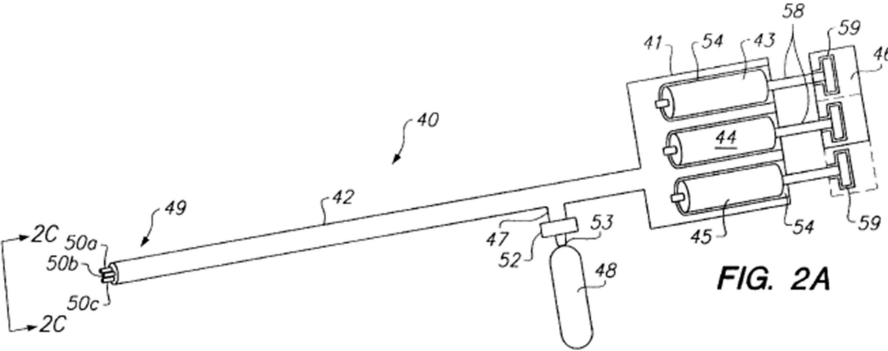
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Thickness is between about 0.5 to 4.0 mm	<p>[7,009,034, c14]: The method of claim 13, comprising choosing the predetermined thickness to be about 0.5 to about 4.0 mm.</p> <p>[7,332,566, c32]</p> <p>[7,592,418, c8]: The method of claim 1 wherein the predetermined thickness is from about 0.5 mm to about 10.0 mm.</p>	<ul style="list-style-type: none">• <u>Gayet & Fortier</u>: [p. 179 table 1] slab thicknesses from 1.4 to 1.8 mm thickness• <u>Tse</u>: Two drops of this material placed over the CSF leak resulted in a prompt cessation of the leak (Fig 1). The adhesive should be applied as a thin film over the prepared site. Applying a thick film does not increase the adhesive strength.• <u>US 5,583,114</u>: A solid TEFLON block was then quickly placed over the sealant prior to cure so that the TEFLON film served as a spacer to create a layer of sealant exactly 0.4 mm thick ... Although the sealant hydrogel swelled to about double in thickness, substantial retention of sealant performance was retained. In all of these applications, the present adhesive composition is a thin layer of cured material which is effectively sandwiched between two adjacent layers of living tissues.• <u>4,839,345</u>: A₈ liquid was added to B₈ liquid, stirred and mixed at room temperature for 10 minutes, and the solution was poured into a polypropylene vessel of 200×250×2 mm of a thickness of 0.6 mm, and warmed for 2 minutes at 50° C.• <u>Bryant (Biomaterials)</u>: Chondrocytes encapsulated in photocrosslinked hydrogels of varying thickness were examined to assess the potential for using photopolymerization technology to tissue engineer cartilaginous tissue in defects of different sizes. We demonstrate the potential for using photopolymerization technology to encapsulate chondrocytes in poly(ethylene oxide) hydrogels, which vary in thickness from 2 to 8 mm.• <u>Champagne</u>: Clinically proven, the toxic degradation products of longer-chain cyanoacrylates are barely detectable on extraction studies, such that they are widely considered non-toxic ... the adhesive was generally sprayed on using a spray gun nozzle and pressurized nitrogen gas, which left a thin, uniform layer of polymer on the tissue surface that dried into a flexible sheet.• <u>Ellis</u>: histoacryl must be applied in spots, in a thin layer only, called spot-welding ... when pressed into a thin film between two adherents.• <u>WO 2000/033764</u>: As described above, advances in modern surgery provide access to the deepest internal organs with minimally invasive surgical devices. As also described above, biocompatible crosslinked polymers that can be formed in situ are useful in such surgical procedures. However, most such formulations, for

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		<p>example, fibrin glue, are colorless, and the amount of material used is typically very small, leading to a film thickness of only about 0.05 to 1 mm.</p> <ul style="list-style-type: none">• <u>Epstein</u>: [EVICEL] should be administered ... in an even thin layer, approximately 1-mm thick.• <u>Davis</u>: A thin line of glue should be applied sparingly over the wound edges, as a large amount may result in thermal damage of the surrounding tissue, and impaired wound healing.• <u>7,279,176</u>: This method is capable of creating uniform polymeric coating of between one and 500 microns in thickness, most preferably about twenty microns, which does not evoke thrombosis or localized inflammation.
Thickness between about 1 mm to about 10 mm	<p>[7,009,034, c17]: The method of claim 16, wherein the predetermined thickness is from about 0.1 mm to about 10.0 mm.</p> <p>[7,332,566, c10]: The polymeric coating of claim 1 wherein the predetermined thickness is from about 0.5 to about 10.0 mm.</p> <p>[7,332,566, c23]</p> <p>[7,592,418, c8]: The method of claim 1 wherein the predetermined thickness is from about 0.5 mm to about 10.0 mm.</p>	<ul style="list-style-type: none">• <u>Tse</u>: Two drops of this material placed over the CSF leak resulted in a prompt cessation of the leak (Fig 1). The adhesive should be applied as a thin film over the prepared site. Applying a thick film does not increase the adhesive strength.• <u>US 5,583,114</u>: A solid TEFLON block was then quickly placed over the sealant prior to cure so that the TEFLON film served as a spacer to create a layer of sealant exactly 0.4 mm thick ... Although the sealant hydrogel swelled to about double in thickness, substantial retention of sealant performance was retained. <p>In all of these applications, the present adhesive composition is a thin layer of cured material which is effectively sandwiched between two adjacent layers of living tissues.</p> <ul style="list-style-type: none">• <u>Gayet & Fortier</u>: [p. 179 table 1] slab thicknesses from 1.4 to 1.8 mm thickness• <u>6,165,201</u>: Water-soluble coatings may form thin films,• <u>Bryant (Biomaterials)</u>: Chondrocytes encapsulated in photocrosslinked hydrogels of varying thickness were examined to assess the potential for using photopolymerization technology to tissue engineer cartilaginous tissue in defects of different sizes. We demonstrate the potential for using photopolymerization technology to encapsulate chondrocytes in poly(ethylene oxide) hydrogels, which vary in thickness from 2 to 8 mm.• <u>Champagne</u>: Clinically proven, the toxic degradation products of longer-chain cyanoacrylates are barely detectable on extraction studies, such that they are widely considered non-toxic ... the adhesive was generally sprayed on using a spray gun nozzle and pressurized nitrogen gas, which left a thin, uniform layer of

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		<p>polymer on the tissue surface that dried into a flexible sheet.</p> <ul style="list-style-type: none">• <u>Ellis</u>: histoacryl must be applied in spots, in a thin layer only, called spot-welding ... when pressed into a thin film between two adherents ... enabling precise control of the quantity and thickness of the adhesive film applied.• <u>Sawhney et al</u>: The gel was removed from the tube and sliced into 2-mm-thick disks.• <u>WO 2000/090897</u>: The regional barriers need not form bulk hydrogels, but may form coatings on tissue upon instillation that may be thin and of the order of 1-1000 microns in thickness.• <u>WO 2000/033764</u>: As described above, advances in modern surgery provide access to the deepest internal organs with minimally invasive surgical devices. As also described above, biocompatible crosslinked polymers that can be formed in situ are useful in such surgical procedures. However, most such formulations, for example, fibrin glue, are colorless, and the amount of material used is typically very small, leading to a film thickness of only about 0.05 to 1 mm.• <u>Epstein</u>: [EVICEL] should be administered ... in an even thin layer, approximately 1-mm thick.• <u>Davis</u>: A thin line of glue should be applied sparingly over the wound edges, as a large amount may result in thermal damage of the surrounding tissue, and impaired wound healing.• <u>7,279,176</u>: This method is capable of creating uniform polymeric coating of between one and 500 microns in thickness, most preferably about twenty microns, which does not evoke thrombosis or localized inflammation.
Visualization agent not covalently linked to hydrogel	[7,332,566, c4]: The polymeric coating of claim 1 wherein the visualization agent is not covalently linked to the hydrogel. [7,332,566, c16] [7,332,566, c28] [7,592,418, c5] [7,592,418, c27]	<ul style="list-style-type: none">• <u>Tse</u>: D&C Violet #2 will not link to hydrogel.• <u>Gayet & Fortier</u>: methylene blue will not link to hydrogel.• <u>2014/0243428</u>: The coating was colored using a dye for easy visualization and the observed color change after healing is caused by its exposure to low-pH buffer. For ease of visualization, the hydrogels were dyed yellow and maroon by soaking them in PBS containing 0.5% (vol/vol) methyl red indicator and approximately 0.002% (wt/vol) alizarin red S, respectively.• <u>Bryant et al</u>: The glycosaminoglycan (GAG) content was determined using the dimethylmethylene blue dye method

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		<ul style="list-style-type: none">• <u>Champagne</u>: Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient’s tissue.• <u>Fleischmann et al. Polymers (2015) v. 7; 717-746</u>: <p>hydrogen bonding, electrostatic interactions, inclusion complexes, ...</p> <p>Figure 2. Schematic illustration of non-covalent dye binding to polymers.</p> <ul style="list-style-type: none">• <u>WO 2000/033764</u>: Where convenient, the biocompatible crosslinked polymer or precursor solutions (or both) may contain visualization agents to improve their visibility during surgical procedures. Visualization agents are especially useful when used in MIS procedures, due among other reasons to their improved visibility on a color monitor. Visualization agents may be selected from among any of the various non-toxic colored substances suitable for use in medical implantable medical devices, such as FD&C dyes 3 and 6, eosin, methylene blue, indocyanine green, or colored dyes normally found in synthetic surgical sutures. The preferred color is green or blue because it has better visibility in presence of blood or on a pink or white tissue background. Red is the least preferred color. The visualization agent may be present in either a crosslinker or functional polymer solution, preferably in a functional polymer solution. The preferred colored substance may or may not become incorporated into the biocompatible crosslinked polymer. Preferably, however, the visualization agent does not have a functional group capable of reacting with the crosslinker or functional polymer.

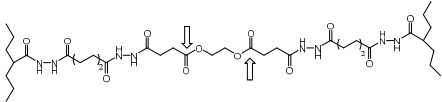
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		<p>The visualization agent may be used in small quantities, preferably less than 1% weight/volume, more preferably less than 0.01% weight/volume and most preferably less than 0.001% weight/volume concentration.</p> <ul style="list-style-type: none"> • <u>Davis</u>: A thin line of glue should be applied sparingly over the wound edges, as a large amount may result in thermal damage of the surrounding tissue, and impaired wound healing. Violet #2 is not covalently linked. • <u>7,279,176</u>: Useful photoinitiators are those which can be used to initiate by free radical generation polymerization of the macromers without cytotoxicity and within a short time frame, minutes at most and most preferably seconds. Preferred dyes as initiators of choice for LWUV initiation are ethyl eosin, 2,2-dimethoxy-2-phenyl acetophenone, other acetophenone derivatives, and camphorquinone. There are several photooxidizable and photoreducible dyes that may be used to initiate polymerization. These include acridine dyes, for example, acriblarine; thiazine dyes, for example, thionine; xanthine dyes, for example, rose bengal; and phenazine dyes, for example, methylene blue. • <u>6,162,241</u>: Useful photoinitiators are those which can be used to initiate by free radical generation polymerization of the macromers without cytotoxicity and within a short time frame, minutes at most and most preferably seconds. Preferred dyes as initiators of choice for LWUV initiation are ethyl eosin, 2,2-dimethoxy-2-phenyl acetophenone, other acetophenone derivatives, and camphorquinone. In all cases, crosslinking and polymerization are initiated among copolymers by a light-activated free-radical polymerization initiator such as 2,2-dimethoxy-2-phenylacetophenone or a combination of ethyl eosin and triethanolamine, for example.
An applicator	[8,003,705, c4]: an applicator; [8,003,705, c4]: wherein the applicator is configured to mix at least the first precursor, the second precursor, and the third precursor to form a crosslinked hydrogel in situ comprising covalent bonds formed by reaction of the functional groups of the precursors and further comprising the at least one isolated hydrolytically degradable ester group;	<ul style="list-style-type: none"> • <u>US 6,051,648 (Rhee)</u>: In order to administer the composition prior to crosslinking, the first synthetic polymer and second synthetic polymer may be contained within separate barrels of a dual-compartment syringe. • Tse: This material is applied in a small presterilized plastic vial. • <u>US 5,614,587 (Rhee)</u>: For example, the collagen and multifunctionally activated synthetic hydrophilic polymer are generally provided in separate syringes, the contents of which are then mixed together using a syringe-to-syringe mixing technique just prior to delivery to a first surface.

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		<ul style="list-style-type: none">• <u>US 5,583,114</u>:The two component adhesive composition of the present invention may be applied to tissue in a number of different ways. For example, the adhesive may be quickly mixed together and then applied using common applicators• <u>6,165,201</u>:  <p>FIG. 2A</p> <ul style="list-style-type: none">• Histoacryl Blue is delivered in sterile plastic capsules that have a fine plastic capillary tube through which adhesive can be applied. There are several applicator tips to choose from, as well as a spray formulation. Histoacryl Blue is named for the blue coloring of the glue, which allows physicians to accurately judge and control the amount of adhesive they apply without tattooing or permanently coloring the patient’s tissue.• <u>Ellis</u>: Histoacryl costs approximately \$23 per tube• <u>US 2006/0062768</u>: The kit 22 may further contain at least one sterile syringe 28 to draw the PEG composition from the vial 24 and deliver the PEG composition to the targeted application site, either topically (e.g., by spraying) or by injection. Further syringes 30 may be included for mixing the PEG composition with additive or auxiliary components, if included.• <u>WO 2000/09087</u>: In accordance with the methods of the present invention, macromer solutions used in forming regional barriers may be instilled by pouring, spraying (e.g., using two or more spray nozzles that simultaneously spray more than one solution into the region of interest) , or by devices such as infusion catheters (e.g., dual lumen catheters or nozzles with mixing tips) ,

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		<ul style="list-style-type: none"> • <u>WO 2000/033764</u>: A Fibriject™ (Micromedics, Inc) 5 cc syringe holder and cap was used, preloaded with 5 cc of each solution and attached to a dual barrel atomizing sprayer. The sprayer has two hubs for the syringes to connect to allowing the two fluids to be advanced through two separate lumens over any preset distance. • <u>Davis</u>: Alternatively a 23 gauge needle can be attached to the stem of the phial, particularly for very fine work (2). Another method used is to cut the long stem of the phial after each application, permitting the phial to be used 5-10 times.
Hydrogel forms within 60 seconds, or; less than 45 seconds	<p>[7,009,034, c9]: The method of claim 1, wherein the hydrogel forms within 60 seconds after contact with the substrate.</p> <p>[7,009,034, c20]: The method of claim 16, wherein the polymer composition crosslinks to form a hydrogel within about 60 seconds after being applied to a substrate.</p> <p>[7,332,566, c6]: The polymeric coating of claim 1 wherein the hydrogel forms within 60 seconds after contact with the substrate.</p> <p>[7,332,566, c18]</p> <p>[7,332,566, c33]</p> <p>[7,332,566, c37] *Note wherein hydrogel is formed when nucleophile is primary amine or primary thiol.</p> <p>[7,592,418, c9]</p> <p>[7,592,418, c29]</p> <p>[6,566,406, c14]: The method of claim 12 wherein the formation of the biocompatible crosslinked polymer requires less than about 45 seconds as measured by a gel time measurement.</p> <p>[6,566,406, c25]: The crosslinked biocompatible material of claim 23 wherein the electrophiles and nucleophiles cause the biocompatible material to have a gel time of less than 120 seconds as measured by a gel time measurement.</p>	<ul style="list-style-type: none"> • <u>US 6,051,648 (Rhee)</u>: the first synthetic polymer and second synthetic polymer may be mixed according to the methods described above prior to delivery to the tissue site, then injected to the desired tissue site immediately (preferably, within about 60 seconds) following mixing. • Tse: two drops of this material placed over the CSF leak resulted in a prompt cessation of the leak; there was an immediate cessation of the CSF leak on application of this material. • <u>US 5,614,587 (Rhee)</u>: See Table 2 – two gel formations are immediate. • <u>US 5,583,114</u>: see Table 1 and Table 2; multiple examples of cure times between 5 and 60 seconds. • <u>Prestwich</u>: Gelation occurred 30-90 seconds after addition of the crosslinker. • <u>Champagne</u>: Polymerization took twenty to thirty seconds. • <u>Ellis</u>: the ethylene molecules are polymerized within seconds. • <u>6,458,147</u>: Within seconds, the liquid material transforms by in situ cross-linking into a non-liquid structure covering the anastomosis. A cross-linked covering structure network formed at room temperature in about 90 seconds. • <u>WO 2000/033764</u>: The crosslinking reactions preferably occur in aqueous solution under physiological conditions. More preferably the crosslinking reactions occur "in situ", meaning they occur at local sites such as on organs or tissues in a living animal or human body. More preferably the crosslinking reactions do not release heat of polymerization. Preferably the crosslinking reaction leading to gelation occurs within 10 minutes, more preferably within 2 minutes, more preferably within one minute, and most preferably within 30 seconds. Preferred electrophilic groups are NHS, SNHS and ENHS (FIG. 9) .

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		<p>Preferred nucleophilic groups are primary amines. The advantage of the NHS-amine reaction is that the reaction kinetics lead to quick gelation usually within 10 minutes, more usually within 1 minute and most usually within 10 seconds. This fast gelation is preferred for in situ reactions on live tissue.</p> <ul style="list-style-type: none">• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddleFifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8. $\text{PEG-COO-R-COO-NHS} + \text{NH}_2\text{-protein} \rightarrow \text{PEG-COO-R-CONH-protein}$• <i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional "double-ester" PEGs, as shown in Scheme 2.• <u>Davis</u>: The wound edges need to be correctly aligned, as correction after polymerization may not be feasible. They should be pressed together for 30 seconds.• <u>WO 97/22371</u>: Alternatively, the first synthetic polymer and second synthetic polymer may be mixed according to the methods described above prior to delivery to the tissue site, then injected to the desired tissue site immediately

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>(preferably, within about 60 seconds) following mixing.</p> <ul style="list-style-type: none"> • <u>6,458,147</u>: Within seconds, the liquid material transforms by in situ cross-linking into a non-liquid structure covering the anastomosis. A cross-linked covering structure network formed at room temperature in about 90 seconds.
<p>Hydrogel forms within 5 seconds; or</p> <p>Less than about 4 seconds</p>	<p>[7,009,034, c10]: The method of claim 1, wherein the hydrogel forms within 5 seconds after contact with the substrate.</p> <p>[7,332,566, c7]: The polymeric coating of claim 1 wherein the hydrogel forms within 5 seconds after contact with the substrate.</p> <p>[7,332,566, c19]</p> <p>[7,332,566, c34]</p> <p>[7,332,566, c38] *Note wherein hydrogel is formed when nucleophile is primary amine or primary thiol.</p> <p>[7,592,418, c10]</p> <p>[7,592,418, c26]</p> <p>[7,592,418, c30]</p> <p>[6,566,406, c15]: The method of claim 12 wherein the formation of the biocompatible crosslinked polymer requires less than about 4 seconds as measured by a gel time measurement.</p> <p>[6,566,406, c25]</p>	<ul style="list-style-type: none"> • Tse: two drops of this material placed over the CSF leak resulted in a prompt cessation of the leak; there was an immediate cessation of the CSF leak on application of the material. • <u>US 5,614,587 (Rhee)</u>: See Table 2 – two gel formations are immediate. • <u>US 5,583,114</u>: see Table 1 and Table 2; multiple examples of cure times between 5 and 60 seconds. • <u>Champagne</u>: Polymerization took twenty to thirty seconds. • <u>Ellis</u>: the ethylene molecules are polymerized within seconds. • <u>WO 2000/033764</u>: The crosslinking reactions preferably occur in aqueous solution under physiological conditions. More preferably the crosslinking reactions occur "in situ", meaning they occur at local sites such as on organs or tissues in a living animal or human body. More preferably the crosslinking reactions do not release heat of polymerization. Preferably the crosslinking reaction leading to gelation occurs within 10 minutes, more preferably within 2 minutes, more preferably within one minute, and most preferably within 30 seconds. Preferred electrophilic groups are NHS, SNHS and ENHS (FIG. 9) . Preferred nucleophilic groups are primary amines. The advantage of the NHS-amine reaction is that the reaction kinetics lead to quick gelation usually within 10 minutes, more usually within 1 minute and most usually within 10 seconds. This fast gelation is preferred for in situ reactions on live tissue. • <u>Davis</u>: The wound edges need to be correctly aligned, as correction after polymerization may not be feasible. They should be pressed together for 30 seconds. • <u>6,458,147</u>: Within seconds, the liquid material transforms by in situ cross-linking into a non-liquid structure covering the anastomosis. A cross-linked covering structure network formed at room temperature in about 90 seconds.
The precursors [<i>including third precursor</i>] are	[8,003,705, c1]: wherein the first biocompatible precursor and the second biocompatible precursor are resistant to enzymatic	<ul style="list-style-type: none"> • <u>US 6,051,648 (Rhee)</u>: Another feature of the invention is that, unlike collagen, the compositions of the invention are not subject to enzymatic cleavage by matrix

Claim element	Patents in which element is found	Relevant Prior Art References
resistant to enzymatic degradation but have hydrolytically labile ester groups	degradation and at least one of the first biocompatible precursor or second biocompatible precursor comprises at least one isolated hydrolytically degradable ester group; and [8,003,705, c11]: wherein at least one of the first, the second, or the third biocompatible precursors comprises at least one isolated hydrolytically degradable ester group; wherein the first, the second, and the third biocompatible precursors are resistant to enzymatic degradation [8,535,705, c1]: (i) the first precursor is selected have <u>only one or two chemically hydrolytically degradable ester bonds per every electrophilic functional group</u> on the first precursor; and	<p>metalloproteinases, such as collagenase, and are therefore not readily degradable in vivo and, as such, are expected to have greater long-term persistence in vivo than prior art collagen compositions.</p> <ul style="list-style-type: none">US 6,051,648 (Rhee): An additional group, represented below as "D", can be inserted between the polymer and the linking group to increase degradation of the crosslinked polymer composition in vivo, for example, for use in drug delivery applications. <p>polymer-D--Q--X+polymer-D-Q-Y→polymer-D--Q--Z--Q--D-polymer-</p> <p>Some useful biodegradable groups "D" include lactide, glycolide, ε-caprolactone, poly(α-hydroxy acid), poly(amino acids), poly(anhydride), and various di- or tripeptides.</p> <ul style="list-style-type: none">US 5,614,587 (Rhee):The structure in Formula 2 results in a conjugate which includes an "ether" linkage which is less subject to hydrolysis. This is distinct from the conjugate shown in Formula 1, wherein an ester linkage is provided. The ester linkage is subject to hydrolysis under physiological conditions.US 5,583,114: Alternatively, the linking moiety may be a readily hydrolyzable compounds such as oligomer derivatives of polylactic acid, polyglycolic acid, polydioxanone, polytrimethylene carbonate, or polycaprolactone as well as copolymers made using suitable monomers of these listed polymers.Prestwich: p.7521, col. 2: The crosslinkers show hydrolytically labile ester groups incorporated into crosslinker backbone (see arrows): <div></div> <p>Additionally, HA hydrogels “would be expected to show increased resistance to degradation in vivo by hyaluronidases.”</p> <ul style="list-style-type: none">6,165,201: it is preferable that the hydrogel system ... be biodegradable.Champagne: if used for a topical wound closure, methyl- and ethylecyanoacrylates degrade slowly enough that there will not be a significant release of toxic breakdown products before the adhesive sloughs off the skin ... The toxic

Claim element	Patents in which element is found	Relevant Prior Art References
		<p>degradation products of longer-chain cyanoacrylates are barely detectable on extraction studies, such that they are widely-considered non-toxic.</p> <ul style="list-style-type: none">• <u>Ellis</u>: In regard to biodegradability, the polymer bonds are hydrolyzed, resulting in formaldehyde and an alkyl cyanoacrylate which is then metabolized and excreted in the urine and feces.• <u>US 2006/0062768</u>: The hydrogel materials gelled within the tissue sites and resided there for thirty days. After thirty days, the materials had all degraded by hydrolysis to various degrees. Composition 3 had entirely degraded. Composition 2 had degraded, but to a lesser extent, with a small amount of material still present. Composition 1 had also degraded, but to a lesser extent than Composition 2, with a larger amount of material still remaining• <u>WO 2000/09087</u>: Degradable Regions The degradable region is selected from any of a variety of polymers that undergo either hydrolytic, enzymatic, or thermal decomposition by bond scission of linkages so as to produce ultimately soluble and physiologically cleared molecules. Preferable biodegradable polymers, oligomers or even single moieties can be selected from the group consisting of poly (-hydroxy acids), poly (lactones) , poly(amino acids), peptide sequences, oligonucleotides, poly (saccharides) , poly (anhydrides) , poly (orthoesters) , poly (phosphazenes) , and poly (phosphoesters) , poly (urethanes) , poly (amides) , poly (imines) , poly (esters) , phosphoester linkages and combinations, copolymers, blends, etc. In some cases the water soluble and the degradable region may be one and the same, for example, in the case of proteins and poly (saccharides) that are degraded by naturally existing enzymes within the body.• <u>WO 2000/033764</u>: The biodegradable linkage may be chemically or enzymatically hydrolyzable or absorbable. Illustrative chemically hydrolyzable biodegradable linkages include polymers, copolymers and oligomers of glycolide, dl- lactide, 1-lactide, caprolactone, dioxanone, and tri ethylene carbonate.• <u>WO 97/22371</u>: An additional group, represented below as "D", can be inserted between the polymer and the linking group to increase degradation of the crosslinked polymer composition in vivo, for example, for use in drug delivery applications.

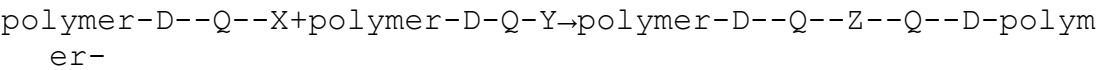
Claim element	Patents in which element is found	Relevant Prior Art References
		<p>polymer - D-Q-X + polymer - D-Q-Y ^ polymer - D-Q-Z-Q-D - polymer –</p> <p>Some useful biodegradable groups "D" include lactide, glycolide, ε-caprolactone, poly(α-hydroxy acid), poly(amino acids), poly(anhydride), and various di- or tripeptides.</p> <p>•</p>

<p>Hydrogel is hydrolytically biodegradable</p>	<p>[7,009,034, c4]: The method of claim 1, wherein the hydrogel is hydrolytically biodegradable.</p> <p>[7,009,034, c15]: The method of claim 13, comprising choosing at least one of the reactive precursor species to have a hydrolytically biodegradable portion such that the hydrogel is biodegradable.</p> <p>[7,332,566, c1]: that is essentially completely degradable in vivo by hydrolytic degradation</p> <p>[7,332,566, c1]: wherein the hydrogel comprises chemical groups that are prone to aqueous hydrolysis and is thereby degradable in vitro by exposure to aqueous solution, and</p> <p>[7,332,566, c12]: wherein the hydrogel comprises chemical groups that are prone to aqueous hydrolysis and is thereby degradable in vitro by exposure to aqueous solution, and</p> <p>[7,332,566, c25]: a biodegradable hydrogel that is essentially completely degradable in vivo by hydrolytic degradation</p> <p>[7,332,566, c25]: wherein the hydrogel comprises chemical groups that are prone to aqueous hydrolysis and is thereby degradable in vitro by exposure to aqueous solution, and</p> <p>[7,592,418, c1]: A method for formulating a polymer composition that crosslinks to form a biodegradable hydrogel that is essentially completely degradable in vivo by hydrolytic degradation,</p> <p>[7,592,418, c1]: wherein the hydrogel comprises chemical groups that are prone to aqueous hydrolysis and are degradable in vitro by exposure to aqueous solution.</p> <p>[6,566,406, c10]: The method of claim 1, wherein providing a synthetic biocompatible functional polymer further comprises providing a synthetic biocompatible functional polymer having a biodegradable link.</p>	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: The structure in FIG. 5 results in a conjugate which includes an "ether" linkage which is less subject to hydrolysis. This is distinct from the conjugate shown in FIG. 4, wherein an ester linkage is provided. The ester linkage is subject to hydrolysis under physiological conditions.• <u>US 5,614,587 (Rhee)</u>: The structure in Formula 2 results in a conjugate which includes an "ether" linkage which is less subject to hydrolysis. This is distinct from the conjugate shown in Formula 1, wherein an ester linkage is provided. The ester linkage is subject to hydrolysis under physiological conditions.• <u>US 5,583,114</u>: Alternatively, the linking moiety may be a readily hydrolyzable compounds such as oligomer derivatives of polylactic acid, polyglycolic acid, polydioxanone, polytrimethylene carbonate, or polycaprolactone as well as copolymers made using suitable monomers of these listed polymers.• <u>6,458,147</u>: In a preferred embodiment of the invention, the material loses its physical strength during the first twenty days, and total resorption occurs in about 4 weeks.• <u>Prestwich</u>: p.7521, col. 2: The crosslinkers show hydrolytically labile ester groups incorporated into crosslinker backbone (see arrows): <div data-bbox="1392 828 2257 1347"><p>FORMULA 1 S-PEG: Difunctional PEG Succinimidyl Glutarate</p><p>collagen-NH₂ collagen-NH₂</p><p>collagen-HN—CO—(CH₂)₃—OC—O—PEG—O—CO—(CH₂)₃—CO—NH—collagen</p></div> <ul style="list-style-type: none">• <u>6,165,201</u>: it is preferable that the hydrogel system ... be biodegradable.
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		<ul style="list-style-type: none">• <u>Champagne</u>: if used for a topical wound closure, methyl- and ethylcyanoacrylates degrade slowly enough that there will not be a significant release of toxic breakdown products before the adhesive sloughs off the skin ... The toxic degradation products of longer-chain cyanoacrylates are barely detectable on extraction studies, such that they are widely-considered non-toxic.• <u>Ellis</u>: In regard to biodegradability, the polymer bonds are hydrolyzed, resulting in formaldehyde and an alkyl cyanoacrylate which is then metabolized and excreted in the urine and feces.• <u>Mei et al.</u>: Most commonly used synthetic polymers to prepare nanoparticles for drug delivery are biodegradable.• <u>US 2006/0062768</u>: The hydrogel materials gelled within the tissue sites and resided there for thirty days. After thirty days, the materials had all degraded by hydrolysis to various degrees. Composition 3 had entirely degraded. Composition 2 had degraded, but to a lesser extent, with a small amount of material still present. Composition 1 had also degraded, but to a lesser extent than Composition 2, with a larger amount of material still remaining• <u>WO 2000/09087</u>: Degradable Regions The degradable region is selected from any of a variety of polymers that undergo either hydrolytic, enzymatic, or thermal decomposition by bond scission of linkages so as to produce ultimately soluble and physiologically cleared molecules. Preferable biodegradable polymers, oligomers or even single moieties can be selected from the group consisting of poly (-hydroxy acids), poly (lactones) , poly(amino acids), peptide sequences, oligonucleotides, poly (saccharides) , poly (anhydrides) , poly (orthoesters) , poly (phosphazenes) , and poly (phosphoesters) , poly (urethanes) , poly (amides) , poly (imines) , poly (esters) , phosphoester linkages and combinations, copolymers, blends, etc. In some cases the water soluble and the degradable region may be one and the same, for example, in the case of proteins and poly (saccharides) that are degraded by naturally existing enzymes within the body.• <u>WO 2000/033764</u>: The biodegradable linkage may be chemically or enzymatically hydrolyzable or absorbable. Illustrative chemically hydrolyzable biodegradable linkages include polymers, copolymers and oligomers of glycolide, dl- lactide, 1-lactide, caprolactone, dioxanone, and tri ethylene carbonate.• <u>Davis</u>: The glue does not need to be removed, it will drop off by itself when the
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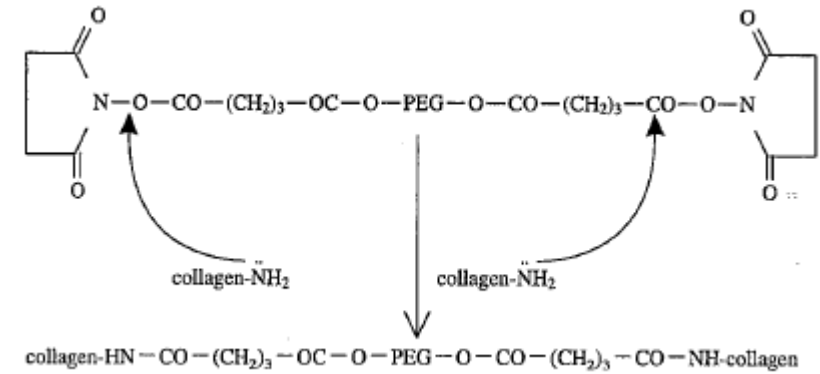
		<p>wound has healed</p> <ul style="list-style-type: none">• <u>7,279,176</u>: Hydrogels releasing or producing NO, most preferably photopolymerizable biodegradable hydrogels capable of releasing physiological amounts of NO for prolonged periods of time, are applied to sites on or in a patient in need of treatment thereof• <u>6,162,241</u>: Biodegradable linkages or polymer or copolymer segments from molecules available in the art may be incorporated into the macromers. The biodegradable region is preferably hydrolyzable under in vivo conditions. In some embodiments, different properties, such as biodegradability and hydrophobicity or hydrophilicity, may be present within the same region of the macromer. Useful hydrolyzable groups include polymers and oligomers of glycolide, lactide, epsilon caprolactone, and other hydroxy acids, and other biologically degradable polymers that yield materials that are non-toxic or present as normal metabolites in the body.• <u>WO 97/22371</u>: An additional group, represented below as "D", can be inserted between the polymer and the linking group to increase degradation of the crosslinked polymer composition in vivo, for example, for use in drug delivery applications. <p>polymer - D-Q-X + polymer - D-Q-Y ^ polymer - D-Q-Z-Q-D - polymer –</p> <p>Some useful biodegradable groups "D" include lactide, glycolide. ε-caprolactone, poly(α-hydroxy acid), poly(amino acids), poly(anhydride), and various di- or tripeptides.</p> <ul style="list-style-type: none">• <u>6,371,975</u>: In a preferred embodiment of the invention, the barrier material loses its physical strength during the first twenty days, and total resorption occurs in about 4 weeks.•
Every ester bond separated by every other ester bond by at least 3 covalent bonds	[8,535,705]: wherein mixing the first and the second synthetic hydrophilic polymer precursors forms crosslinking covalent bonds that are reaction products of the electrophilic and the nucleophilic groups, wherein essentially every ester bond in the	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: An additional group, represented below as "D", can be inserted between the polymer and the linking group to increase degradation of the crosslinked polymer composition in vivo, for example, for use in drug delivery applications.

hydrogel is separated from other ester bonds in the hydrogel by at least three covalent bonds when the hydrogel is formed.



Some useful biodegradable groups "D" include lactide, glycolide, ε-caprolactone, poly(α-hydroxy acid), poly(amino acids), poly(anhydride), and various di- or tripeptides.

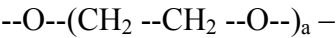
- US 5,614,587 (Rhee): Resulting product has ester groups separated by PEG polymer:



- US 5,583,114: A variety of suitable crosslinking agents may be used in the present invention. Preferred crosslinking agents include a polyethylene glycol or polyoxyethylene chain portion (--PEG--), an activated leaving group portion (--G) and a linking moiety (--LM--) which binds the --PEG-- portion and the leaving group portion --G. Crosslinking agents include compounds of the formula

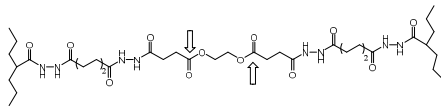


in which --PEG-- is a diradical fragment represented by the formula

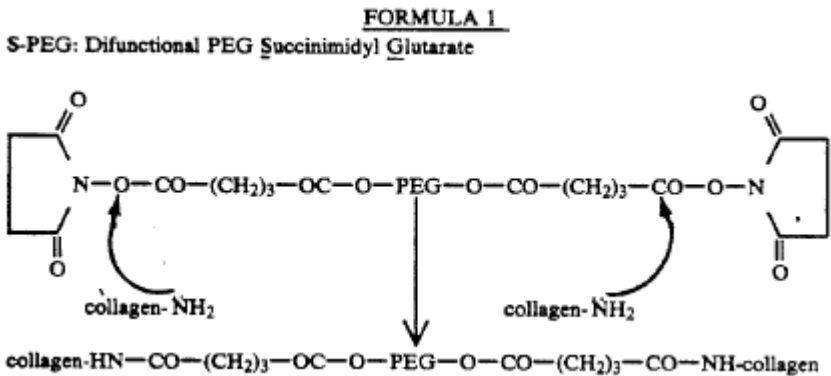


where a is an integer from 20-300; --LM-- is also a diradical fragment such as a carbonate diradical represented by the formula, --C(O)--, a monoester diradical represented by the formula, --(CH₂)_b C(O)-- where b is an integer from 1-5, a diester diradical represented by the formula, --C(O)--(CH₂)_c --C(O)-- where c is an integer from 2-10 and where the aliphatic portion of the radical may be saturated or unsaturated

- Prestwich: p.7521, col. 2: The crosslinkers show hydrolytically labile ester groups incorporated into crosslinker backbone (see arrows):



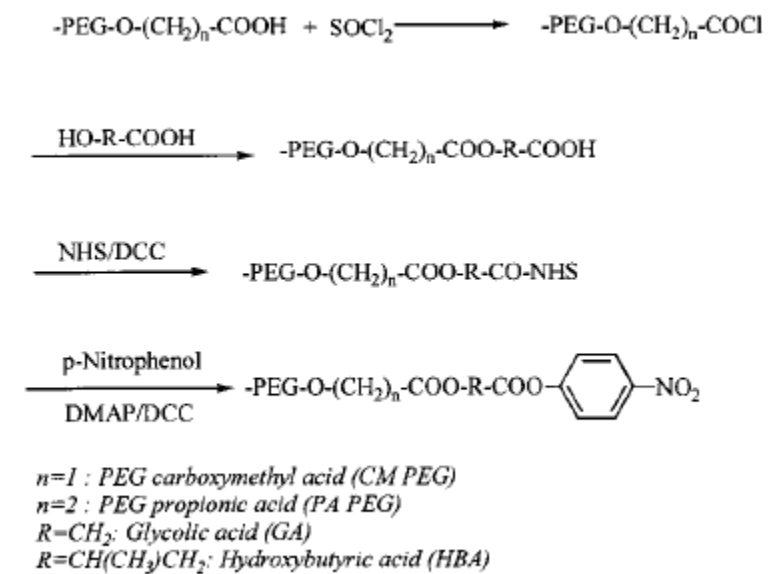
- 5,328,955: PEG group has ester linkages within backbone.



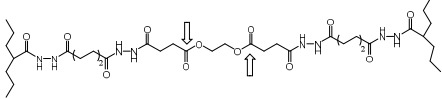
- US 2006/0062768: EXAMPLE 1 Poly(Anhydride Ester) (PAE) SynthesisThe poly(anhydride ester) (PAE) is thereafter derivatized (i.e., functionalized) to include electrophilic function groups. The following reaction Examples 2 and 3, illustrate two methods of functionalization of polyanhydride esters. The hydrogel materials gelled within the tissue sites and resided there for thirty days. After thirty days, the materials had all degraded by hydrolysis to various degrees.

Composition 3 had entirely degraded. Composition 2 had degraded, but to a lesser extent, with a small amount of material still present. Composition 1 had also degraded, but to a lesser extent than Composition 2, with a larger amount of material still remaining.

- Zhao: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the Middle Fifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/mL) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8.



		<p><i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.</p> <ul style="list-style-type: none">• <u>7,279,176</u>: The polymerizable regions are separated by at least one degradable region to facilitate uniform degradation in vivo. There are several variations of these polymers. For example, the polymerizable regions can be attached directly to degradable extensions or indirectly via water soluble nondegradable sections so long as the polymerizable regions are separated by a degradable section. Polyesters (Holland et al., 1986 Controlled Release, 4:155-180) of α-hydroxy acids (viz., lactic acid, glycolic acid), are the most widely used biodegradable materials for applications ranging from closure devices (sutures and staples) to drug delivery systems• <u>WO 97/22371</u>: An additional group, represented below as "D", can be inserted between the polymer and the linking group to increase degradation of the crosslinked polymer composition in vivo, for example, for use in drug delivery applications. <p>polymer - D-Q-X + polymer - D-Q-Y ^ polymer - D-Q-Z-Q-D - polymer –</p> <p>Some useful biodegradable groups "D" include lactide, glycolide, ϵ-caprolactone, poly(α-hydroxy acid), poly(amino acids), poly(anhydride), and various di- or tripeptides.</p> <ul style="list-style-type: none">• <u>6,458,147</u>: In a preferred embodiment of the invention, the material loses its physical strength during the first twenty days, and total resorption occurs in about 4 weeks.•
Hydrogel is degradable in less than about 180 days	[8,003,705, c1]: mixing at least the first biocompatible precursor and the second biocompatible precursor in situ to form a device comprising a crosslinked hydrogel that comprises covalent bonds formed by reaction of the functional groups of	<ul style="list-style-type: none">• <u>US 5,583,114</u>: When the two parts of the mixture are combined, the mixture is initially a liquid which cures in vivo on the surface of tissue in less than about one minute to give a strong, flexible, pliant substantive composition which bonds to the tissue and is absorbed in about four to sixty days.

	<p>the first biocompatible precursor and second biocompatible precursor with each other and further comprising the at least one isolated hydrolytically degradable ester group; wherein the crosslinked hydrogel is resistant to enzymatic degradation, is degradable by hydrolysis of the at least one isolated hydrolytically degradable ester group so that the device is degradable in less than about 180 days,</p> <p>[8,003,705, c1]: wherein the kit further comprises instructions that comprise directions for making a hydrogel that is degradable in an amount of time, with the amount of time being less than about 180 days.</p> <p>[8,003,705, c11]: wherein the hydrogel comprises a sufficient number of the at least one isolated hydrolytically degradable ester groups in the crosslinked hydrogel so that the crosslinked hydrogel is degradable in less than about 180 days and is degradable by hydrolysis of the at least one isolated hydrolytically degradable ester group.</p> <p>[8,535,705 c1]: wherein the biodegradable groups of the hydrogel consist of the esters and the hydrogel as placed in situ in the patient is essentially fully degradable in a patient in less than about 180 days, and</p>	<ul style="list-style-type: none">• <u>Prestwich</u>: p.7521, col. 2: The crosslinkers show hydrolytically labile ester groups incorporated into crosslinker backbone (see arrows):  Variations in crosslinkers... could be potentially exploited in biomaterial design.• <u>Champagne</u>: if used for a topical wound closure, methyl- and ethylcyanoacrylates degrade slowly enough that there will not be a significant release of toxic breakdown products before the adhesive sloughs off the skin ... The toxic degradation products of longer-chain cyanoacrylates are barely detectable on extraction studies, such that they are widely-considered non-toxic.• <u>Ellis</u>: In regard to biodegradability, the polymer bonds are hydrolyzed, resulting in formaldehyde and an alkyl cyanoacrylate which is then metabolized and excreted in the urine and feces.• <u>Sawhney et al</u>: The 10KG5 and the 20KG10 gels partially degraded within 1 day and upon equilibration were already significantly degraded.• <u>US 2006/0062768</u>: EXAMPLE 1 Poly(Anhydride Ester) (PAE) SynthesisThe poly(anhydride ester) (PAE) is thereafter derivatized (i.e., functionalized) to include electrophilic function groups. The following reaction Examples 2 and 3, illustrate two methods of functionalization of polyanhydride esters. The hydrogel materials gelled within the tissue sites and resided there for thirty days. After thirty days, the materials had all degraded by hydrolysis to various degrees. Composition 3 had entirely degraded. Composition 2 had degraded, but to a lesser extent, with a small amount of material still present. Composition 1 had also degraded, but to a lesser extent than Composition 2, with a larger amount of material still remaining.• <u>WO 2000/09087</u>: Several methods for the formation of regional adhesion barriers are described, in which any of a variety of water soluble macromeric precursors are used. The term "macromeric precursor" or "macromer" is meant to connote an oligomeric or polymeric molecule that contains functional groups that enable further polymerization. Preferably the functionality of a macromer molecule is >1 so that a crosslinked network or hydrogel results upon polymerization. Hydrogels that resorb or degrade over a period of time are preferred, and more preferably,
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		<p>those that resorb within one or a few months.</p> <ul style="list-style-type: none">• <u>WO 2000/033764</u>: Thus, it is possible to construct a hydrogel with a desired degradation profile, from a few days to months, using a proper degradable segment.• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the Middle Fifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8. <i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2. ½ lives of the hydrogels range from >500 to 5 days. <u>Davis</u>: The glue does not need to be removed, it will drop off by itself when the wound has healed• <u>7,279,176</u>: FIG. 4 is a graph showing the temporal release (% NO released over time in days) of NO from acryloyl-PEG-Lys5-NO hydrogels at pH 7.4 (circles) and pH 3 (squares).• <u>6,162,241</u>: Biodegradable linkages or polymer or copolymer segments from molecules available in the art may be incorporated into the macromers. The biodegradable region is preferably hydrolyzable under in vivo conditions. In some embodiments, different properties, such as biodegradability and hydrophobicity or hydrophilicity, may be present within the same region of the macromer. Useful hydrolyzable groups include polymers and oligomers of glycolide, lactide, epsilon caprolactone, and other hydroxy acids, and other biologically degradable polymers that yield materials that are non-toxic or present as normal metabolites in the body.
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		<ul style="list-style-type: none">• <u>WO 97/22371</u>: An additional group, represented below as "D", can be inserted between the polymer and the linking group to increase degradation of the crosslinked polymer composition in vivo, for example, for use in drug delivery applications. polymer - D-Q-X + polymer - D-Q-Y ^ polymer - D-Q-Z-Q-D - polymer – Some useful biodegradable groups "D" include lactide, glycolide, ε-caprolactone, poly(α-hydroxy acid), poly(amino acids), poly(anhydride), and various di- or tripeptides.• <u>6,458,147</u>: In a preferred embodiment of the invention, the material loses its physical strength during the first twenty days, and total resorption occurs in about 4 weeks.•
Crosslinked hydrogel degrades in less than about 90, less than about 45 days	<p>[8,003,705, c6]: The kit of claim 4 wherein the amount of time is less than about 90 days.</p> <p>[8,003,705, c7]: The kit of claim 4 wherein the amount of time is less than about 45 days.</p> <p>[8,003,705, c13]</p> <p>[8,003,705, c14]</p> <p>[8,535,705, c17]: The method of claim 1 wherein the hydrogel is essentially fully degradable in a patient in less than about 90 days.</p>	<ul style="list-style-type: none">• <u>US 5,583,114</u>: When the two parts of the mixture are combined, the mixture is initially a liquid which cures in vivo on the surface of tissue in less than about one minute to give a strong, flexible, pliant substantive composition which bonds to the tissue and is absorbed in about four to sixty days.• <u>Ellis</u>: In regard to biodegradability, the polymer bonds are hydrolyzed, resulting in formaldehyde and an alkyl cyanoacrylate which is then metabolized and excreted in the urine and feces.• <u>Sawhney et al</u>: The 10KG5 and the 20KG10 gels partially degraded within 1 day and upon equilibration were already significantly degraded.

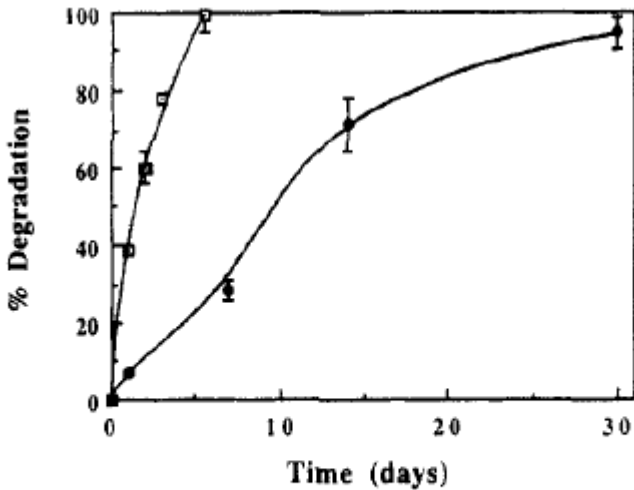


Figure 5. Degradation kinetics for the 4KG5 (◆) and 20KL10 (◻) hydrogels formed by polymerization with LWUV light. Degradation was in HEPES-buffered saline, pH 7.3.

- US 2006/0062768: EXAMPLE 1 Poly(Anhydride Ester) (PAE) SynthesisThe poly(anhydride ester) (PAE) is thereafter derivatized (i.e., functionalized) to include electrophilic function groups. The following reaction Examples 2 and 3, illustrate two methods of functionalization of polyanhydride esters. The hydrogel materials gelled within the tissue sites and resided there for thirty days. After thirty days, the materials had all degraded by hydrolysis to various degrees. Composition 3 had entirely degraded. Composition 2 had degraded, but to a lesser extent, with a small amount of material still present. Composition 1 had also degraded, but to a lesser extent than Composition 2, with a larger amount of material still remaining.
- WO 2000/09087: Several methods for the formation of regional adhesion barriers are described, in which any of a variety of water soluble macromeric precursors are used. The term "macromeric precursor" or "macromer" is meant to connote an oligomeric or polymeric molecule that contains functional groups that enable further polymerization. Preferably the functionality of a macromer molecule is >1

		<p>so that a crosslinked network or hydrogel results upon polymerization. Hydrogels that resorb or degrade over a period of time are preferred, and more preferably, those that resorb within one or a few months.</p> <ul style="list-style-type: none">• <u>WO 2000/033764</u>: Thus, it is possible to construct a hydrogel with a desired degradation profile, from a few days to months, using a proper degradable segment.• <u>Zhao</u>: The second type of hydrogel was formed under mild condition (aqueous solution and room temperature) via a two-step process in which an ester-containing active PEG derivative is first synthesized and then coupled to an amine cross-linker ... A Two-Step Gel Made from Difunctional PEG-Succinimidyl Carbonate Containing an Ester in the MiddlesFifty milligrams of difunctional ester-containing PEG-succinimidyl carbonate 6800 (vide infra) was dissolved in 0.3 mL of deionized water. To the solution was added 0.3 mL of a buffered solution with or without FITC-BSA (10 mg/m) and 0.13 mL of 8-arm PEG-amine (250 mg/mL). After vigorous shaking, the solution was allowed to sit. The gel formed in a few minutes. A suitable pH range was 5.5 to 8. <p><i>Two-Step PEG Hydrogels</i> In preparing a two-step hydrogel, an ester-containing amine-reactive PEG is first synthesized and then coupled to an amine cross-linker. Two types of ester-containing amine-reactive PEGs were synthesized. The first type was prepared from difunctional “double-ester” PEGs, as shown in Scheme 2.</p> <ul style="list-style-type: none">• $\frac{1}{2}$ lives of the hydrogels range from >500 to 5 days.• <u>Davis</u>: The glue does not need to be removed, it will drop off by itself when the wound has healed• <u>7,279,176</u>: FIG. 4 is a graph showing the temporal release (% NO released over time in days) of NO from acryloyl-PEG-Lys5-NO hydrogels at pH 7.4 (circles) and pH 3 (squares).• <u>6,162,241</u>: Biodegradable linkages or polymer or copolymer segments from molecules available in the art may be incorporated into the macromers. The biodegradable region is preferably hydrolyzable under in vivo conditions. In some embodiments, different properties, such as biodegradability and hydrophobicity or hydrophilicity, may be present within the same region of the macromer. Useful hydrolyzable groups include polymers and oligomers of glycolide, lactide, epsilon caprolactone, and other hydroxy acids, and other biologically degradable
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		<p>polymers that yield materials that are non-toxic or present as normal metabolites in the body.</p> <ul style="list-style-type: none">• <u>WO 97/22371</u>: An additional group, represented below as "D", can be inserted between the polymer and the linking group to increase degradation of the crosslinked polymer composition in vivo, for example, for use in drug delivery applications. <p>polymer - D-Q-X + polymer - D-Q-Y ^ polymer - D-Q-Z-Q-D - polymer –</p> <p>Some useful biodegradable groups "D" include lactide, glycolide, ε-caprolactone, poly(α-hydroxy acid), poly(amino acids), poly(anhydride), and various di- or tripeptides.</p> <ul style="list-style-type: none">• <u>6,458,147</u>: In a preferred embodiment of the invention, the material loses its physical strength during the first twenty days, and total resorption occurs in about 4 weeks.•
Biodegradable hydrogel is adherent to the tissue	<p>[7,009,034, c11]: The method of claim 1, wherein the biodegradable hydrogel is adherent to the tissue. [7,332,566, c20] [7,332,566, c30] [7,592,418, c5]: The method of claim 1 wherein the biodegradable hydrogel is adherent to the substrate. [7,592,418, c24] [7,592,418, c28] [7,009,034, c12]: A hydrogel composition adapted for use with a tissue of a patient, the composition being made by the process of claim 11.</p>	<ul style="list-style-type: none">• <u>US 5,614,587 (Rhee)</u>: In a general method for effecting the attachment of a first surface to a second surface: 1) collagen and a multifunctionally activated synthetic hydrophilic polymer are provided; 2) the collagen and synthetic polymer are mixed together to initiate crosslinking between the collagen and the synthetic polymer; 3) the collagen--synthetic polymer mixture is applied to a first surface before substantial crosslinking has occurred between the collagen and the synthetic polymer; and 4) the first surface is contacted with a second surface to effect adhesion between the first surface and the second surface. At least one of the first and second surfaces is preferably a native tissue surface.• <u>US 5,583,114</u>: When the two parts of the mixture are combined, the mixture is initially a liquid which cures in vivo on the surface of tissue in less than about one minute to give a strong, flexible, pliant substantive composition which bonds to the tissue.• <u>Gayet & Fortier</u>: We believe that this family of BSA-PEG hydrogels could be useful for the preparation of controlled release devices in the field of wound dressing.

		<ul style="list-style-type: none">• <u>Champagne</u>: It was well known that these adhesives formed strong bonds with human skin.• <u>Ellis & Shaikh</u>: Fibrin glue, since the early 1970s, has gained popularity as a biologic adhesive amount the surgical specialties, and has been reported to be a safe bioadhesive and sealant ... We have been using histoacryl glue for closure of surgical incisions in facial and plastic reconstructive surgery.• <u>Sawhney et al., Macromolecules, (1993) 26, 581-587</u>: Macromers having a poly(ethylene glycol) central block, extended with oligomers of a-hydroxy acids such as oligo(dl-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation of cross-linked gels. These gels degrade upon hydrolysis of the oligo(a-hydroxy acid) regions into poly(ethylene glycol), the a-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular drug delivery.• <i>WO 2000/09087: Title: METHODS FOR FORMING REGIONAL TISSUE ADHERENT BARRIERS AND DRUG DELIVERY SYSTEMS</i>• <u>WO 2000/033764</u>: Biocompatible crosslinked polymers, and methods for their preparation and use, are disclosed in which the biocompatible crosslinked polymers are formed from water soluble precursors having electrophilic and nucleophilic groups capable of reacting and crosslinking in situ. Methods for making the resulting biocompatible crosslinked polymers biodegradable or not are provided, as are methods for controlling the rate of degradation. The crosslinking reactions may be carried out in situ on organs or tissues or outside the body. Applications for such biocompatible crosslinked polymers and their precursors include controlled delivery of drugs, prevention of post-operative adhesions, coating of medical devices such as vascular grafts, wound dressings and surgical sealants.• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples
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		<p>in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).” BioGlue’s two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.</p> <ul style="list-style-type: none">• <u>Davis</u>: The glue does not need to be removed, it will drop off by itself when the wound has healed• <u>7,279,176</u>: In a particularly preferred application of these macromers, an ultrathin coating is applied to the surface of a tissue, most preferably the lumen of a tissue such as a blood vessel. One use of such a coating is in the treatment or prevention of restenosis, abrupt reclosure, or vasospasm after vascular intervention. An initiator is applied to the surface of the tissue, allowed to react, adsorb or bond to tissue, the unbound initiator is removed by dilution or rising, and the macromer solution is applied and polymerized. This method is capable of creating uniform polymeric coating of between one and 500 microns in thickness, most preferably about twenty microns, which does not evoke thrombosis or localized inflammation..• <u>6,162,241</u>: A method of controlling hemostasis by applying a hemostatic agent in a tissue sealant composition. The tissue sealant is a biodegradable, biocompatible synthetic polymer that may not intrinsically possess strong hemostatic properties.• <u>WO 97/22371</u>: We have found that the preferred compositions of the invention tend to have unusually high tackiness, making them particularly suitable for use as bioadhesives, for example, for use in surgery.•
Medical condition is wound covering, tissue sealing, tissue coating	<p>[8,535,705, c5]: The method of claim 1 wherein the medical condition is wound covering.</p> <p>[8,535,705, c6]: The method of claim 1 wherein the medical condition is tissue sealing.</p> <p>[8,535,705, c7]: The method of claim 1 wherein the medical condition is tissue coating.</p>	<ul style="list-style-type: none">• <u>US 6,051,648 (Rhee)</u>: The crosslinked polymer compositions of the invention can also be used for augmentation of soft or hard tissue within the body of a mammalian subject.• <u>Tse</u>: Butyl-2-cyanoacrylate tissue adhesive successfully sealed three cases of CSF leaks encountered during orbital surgery. The application of tissue adhesive was followed by prompt cessation of the leak.• <u>US 5,614,587 (Rhee)</u>: Collagen-based compositions useful in the attachment of tissues, or the attachment of tissues to synthetic implant materials, are disclosed.• <u>US 5,583,114</u>: This invention is related to an adhesive composition which may be used to bond or seal tissue in vivo.• <u>Gayet & Fortier</u>: We believe that this family of BSA-PEG hydrogels could be

		<p>useful for the preparation of controlled release devices in the field of wound dressing.</p> <ul style="list-style-type: none">• <u>2014/0243428</u>: The disclosure provides for self-healing hydrogels, complex structures made therefrom, and use thereof, including use of the hydrogels as self-healing coatings, self-healing sealants, tissue adhesives, and drug carriers.• <u>4,839,345</u>: This invention relates to hydrated adhesive gels, especially hydrated adhesive gels for a self-adhesion cataplasm and pack agents having sheet shape.• <u>5,328,955</u>: The conjugates and compositions containing the conjugates can be coated on to various medical devices, including catheters, bone implants, and platinum wires to treat aneurysms.• <u>6,165,201</u>: it is an object of the present invention to provide apparatus and methods that enable a tissue coating comprising two or more crosslinkable fluids to be applied in situ as a spray.• <u>Champagne</u>: [p. 162]: Cyanoacrylates used to quickly stop bleeding; cyanoacrylate tissue adhesives.• <u>Ellis & Shaikh</u>: Fibrin glue, since the early 1970s, has gained popularity as a biologic adhesive amount the surgical specialties, and has been reported to be a safe bioadhesive and sealant ... We have been using histoacryl glue for closure of surgical incisions in facial and plastic reconstructive surgery.• <u>Sawhney et al., Macromolecules, (1993) 26, 581-587</u>: Macromers having a poly(ethylene glycol) central block, extended with oligomers of a-hydroxy acids such as oligo(dl-lactic acid) or oligo(glycolic acid) and terminated with acrylate groups, were synthesized and characterized with the goal of obtaining a bioerodible hydrogel that could be formed in direct contact with tissues ... Due to the multifunctionality of the macromers, polymerization results in the formation of cross-linked gels. These gels degrade upon hydrolysis of the oligo(a-hydroxy acid) regions into poly(ethylene glycol), the a-hydroxy acid, and oligo(acrylic acid) ... If polymerized in contact with tissues, the gels adhere to the tissues, presumably by interpenetration ... These novel materials are suitable for a number of biomedical applications and show potential for use in macromolecular drug delivery.• <u>WO 2000/09087</u>: It is another object of this invention to provide in situ formation of regional barriers by macromere solutions at concentrations close to equilibrium
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		<p>hydration levels, to reduce or prevent post-surgical adhesion formation.</p> <ul style="list-style-type: none">• <u>WO 2000/033764</u>: Biocompatible crosslinked polymers, and methods for their preparation and use, are disclosed in which the biocompatible crosslinked polymers are formed from water soluble precursors having electrophilic and nucleophilic groups capable of reacting and crosslinking in situ. Methods for making the resulting biocompatible crosslinked polymers biodegradable or not are provided, as are methods for controlling the rate of degradation. The crosslinking reactions may be carried out in situ on organs or tissues or outside the body. Applications for such biocompatible crosslinked polymers and their precursors include controlled delivery of drugs, prevention of post-operative adhesions, coating of medical devices such as vascular grafts, wound dressings and surgical sealants.• <u>Epstein</u>: BioGlue Surgical Adhesive is a surgical sealant indicated for use as an adjunct to standard methods of achieving hemostasis such as sutures and staples in adult patients in open surgical repair of large vessels (such as aorta, femoral, and carotid arteries).'' BioGlue's two components, purified bovine serum albumin and glutaraldehyde, when mixed together polymerize in 20 to 30 seconds.• <u>5,292,362</u>: The present invention is directed to a composition adapted to bond separated tissues together or to coat tissues or prosthetic materials to enhance strength and water tightness preferably upon the application of energy and particularly to a composition which is activated by a laser to form a strong, biologically compatible bond or coating.• <u>Zhao</u>: Hydrogels are generally considered as biocompatible materials because of their high water content. They have been used in a variety of biomaterial and biotechnology applications, such as tissue engineering, artificial organs, and drug delivery.• <u>Davis</u>: One product widely used in A&E departments contains a non-toxic blue dye which enables visualisation of the quantity applied. Surgical glue may be used as an alternative, or adjunct to more traditional methods of wound closure, such as sutures, staples, and wound closure ships.• <u>7,279,176</u>: In a particularly preferred application of these macromers, an ultrathin coating is applied to the surface of a tissue, most preferably the lumen of a tissue such as a blood vessel. One use of such a coating is in the treatment or prevention
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		<p>of restenosis, abrupt reclosure, or vasospasm after vascular intervention. An initiator is applied to the surface of the tissue, allowed to react, adsorb or bond to tissue, the unbound initiator is removed by dilution or rising, and the macromer solution is applied and polymerized. This method is capable of creating uniform polymeric coating of between one and 500 microns in thickness, most preferably about twenty microns, which does not evoke thrombosis or localized inflammation.</p> <ul style="list-style-type: none">• <u>6,162,241</u>: A method of controlling hemostasis by applying a hemostatic agent in a tissue sealant composition. The tissue sealant is a biodegradable, biocompatible synthetic polymer that may not intrinsically possess strong hemostatic properties.• <u>WO 97/22371</u>: In a general method for augmenting soft or hard tissue within the body of a mammalian subject, a first synthetic polymer containing two or more nucleophilic groups and a second synthetic polymer containing two or more electrophilic groups are administered simultaneously to a tissue site in need of augmentation and the reaction mixture is allowed to crosslink in situ to effect augmentation of the tissue.• <u>6,371,975</u>: A biocompatible and biodegradable barrier material is applied to a tissue region, e.g., to seal a vascular puncture site. The barrier material comprises a compound, which is chemically cross-linked without use of an enzyme to form a non-liquid mechanical matrix. The compound preferably includes a protein comprising recombinant or natural serum albumin, which is mixed with a polymer that comprises poly(ethylene) glycol (PEG), and, most preferably, a multi-armed PEG polymer.• <u>6,458,147</u>: The liquid material transforms as it is being dispersed as a result of cross-linking into an in situ-formed non-liquid covering structure. The covering structure intimately adheres and conforms to the surface the compromised tissue region, as FIG. 3 best shows.• <u>Otani</u>: In this study, a rapidly curable hydrogel glue was prepared as the seal for lung air leak. Mixing an aqueous solution of gelatin and poly(l-glutamic acid) with a water soluble carbodiimide produced a hydrogel. The mixed gelatin and PLGA aqueous solution sets in several seconds to a hydrogel at 37 °C with the addition of WSC; this is as short as conventional fibrin glue.
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Exhibit 10

1 IN THE UNITED STATES DISTRICT COURT
2 FOR THE DISTRICT OF DELAWARE
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4 - - - - - X
5 INTEGRA LIFESCIENCES CORP., :
6 INTEGRA LIFESCIENCES SALES LLC, : Civil Action No.
7 CONFLUENT SURGICAL, INC. AND : 15-819 (LPS)
8 INCEPT LLC, :
9 Plaintiffs, :
10 vs. :
11 HYPERBRANCH MEDICAL TECHNOLOGY, :
12 INC., :
13 Defendant. :
14 - - - - - X
15
16 Videotape Deposition of DENNIS J. RIVET, II, M.D.
17 Washington, D.C.
18 Friday, October 27, 2017
19 9:00 a.m.
20 Job No. WDC-149043
21 Pages: 1 - 386
22 Reported by: Dana C. Ryan, RPR, CRR

DENNIS J. RIVET, II, M.D. - 10/27/2017

Pages 2..5

<p style="text-align: right;">Page 2</p> <p>1</p> <p>2</p> <p>3</p> <p>4</p> <p>5 October 27, 2017</p> <p>6 9:00 a.m.</p> <p>7</p> <p>8</p> <p>9</p> <p>10 Videotape Deposition of DENNIS J.</p> <p>11 RIVET, II, M.D., held at the law offices of Banner</p> <p>12 & Witcoff, Ltd., 1100 13th Street, Northwest,</p> <p>13 Suite 1200, Washington, D.C., before Dana C. Ryan,</p> <p>14 Registered Professional Reporter, Certified</p> <p>15 Realtime Reporter and Notary Public in and for the</p> <p>16 District of Columbia, who officiated in</p> <p>17 administering the oath to the witness.</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p>	<p style="text-align: right;">Page 4</p> <p>1 Also present:</p> <p>2 David Cooper, Videographer</p> <p>3</p> <p>4</p> <p>5</p> <p>6</p> <p>7</p> <p>8</p> <p>9</p> <p>10</p> <p>11</p> <p>12</p> <p>13</p> <p>14</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p>
<p style="text-align: right;">Page 3</p> <p>1 A P P E A R A N C E S</p> <p>2</p> <p>3 ON BEHALF OF THE PLAINTIFFS:</p> <p>4 ROBERT F. ALTHERR, JR., Esquire</p> <p>5 Banner & Witcoff, Ltd.</p> <p>6 1100 13th Street, Northwest</p> <p>7 Suite 1200</p> <p>8 Washington, D.C. 20005</p> <p>9 Telephone: 202.284.3000</p> <p>10 Email: raltherr@bannerwitcoff.com</p> <p>11</p> <p>12 ON BEHALF OF THE DEFENDANT:</p> <p>13 JAMES P. HUGHES, Esquire</p> <p>14 ADAM PIVOVAR, Esquire</p> <p>15 Cooley LLP</p> <p>16 1299 Pennsylvania Avenue, Northwest</p> <p>17 Suite 700</p> <p>18 Washington, D.C. 20004</p> <p>19 Telephone: 202.842.7800</p> <p>20 Email: jhughes@cooley.com</p> <p>21 Email: apivovar@cooley.com</p> <p>22</p>	<p style="text-align: right;">Page 5</p> <p>1 C O N T E N T S</p> <p>2 EXAMINATION OF DENNIS J. RIVET, II, M.D.: PAGE:</p> <p>3 By Mr. Hughes 7</p> <p>4</p> <p>5</p> <p>6</p> <p>7 E X H I B I T S</p> <p>8 (Attached to the Transcript)</p> <p>9 DEPOSITION PAGE:</p> <p>10 Exhibit 411 Expert Report Of 90</p> <p>11 Dr. Dennis J. Rivet</p> <p>12 Exhibit 412 Rebuttal Expert Report Of 302</p> <p>13 Dr. Dennis J. Rivet</p> <p>14 Exhibit 413 Screenshots From The Video 368</p> <p>15 Titled Adherus AutoSpray</p> <p>16 Following Temporal Lobectomy</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p>

<p style="text-align: right;">Page 6</p> <p>1 PROCEEDINGS</p> <p>2 THE VIDEOGRAPHER: Here begins video</p> <p>3 disk number 1 in the video deposition of Dennis</p> <p>4 Rivet, M.D., in the matter of Integra LifeScience</p> <p>5 [sic] Corporation, Integra LifeSciences Sales LLC,</p> <p>6 Confluent Surgical, Inc. and Incept LLC versus</p> <p>7 HyperBranch Medical Technology, in the United</p> <p>8 States District Court for the District of</p> <p>9 Delaware, Case Number 15-819 (LPS).</p> <p>10 Today is Friday, October 27, 2017. The</p> <p>11 time on the video monitor is approximately 22</p> <p>12 seconds past 9:00 a.m. We are now on the record.</p> <p>13 My name is David Cooper. I'm the</p> <p>14 certified legal video specialist with DTI Court</p> <p>15 Reporting Solutions, 1875 I Street, Northwest,</p> <p>16 Suite 802, Washington, D.C. 20006. This</p> <p>17 deposition is taking place at Banner & Witcoff</p> <p>18 located at 1100 13th Street, Northwest, Suite</p> <p>19 1200, Washington, D.C. 20005, in the conference</p> <p>20 Room 12A.</p> <p>21 Would counsel and all present please</p> <p>22 introduce themselves and who they represent?</p>	<p style="text-align: right;">Page 8</p> <p>1 Q And have you ever been deposed before,</p> <p>2 Dr. Rivet?</p> <p>3 A Yes.</p> <p>4 Q Approximately how many times have you</p> <p>5 been deposed?</p> <p>6 A Three.</p> <p>7 Q When was the last time you were</p> <p>8 deposed?</p> <p>9 A Approximately 2012.</p> <p>10 Q And what was the topic of that</p> <p>11 deposition?</p> <p>12 A It was a injury suit of a patient of</p> <p>13 mine I believe brought against their employer.</p> <p>14 Q And what type of injury was at issue in</p> <p>15 that case?</p> <p>16 A A spine injury.</p> <p>17 Q And it was a spine injury that the</p> <p>18 person incurred on the job?</p> <p>19 A Correct.</p> <p>20 Q Okay. And when was the second-to-last</p> <p>21 time you were deposed?</p> <p>22 A 2008, approximately.</p>
<p style="text-align: right;">Page 7</p> <p>1 MR. ALTHERR: Robert F. Altherr, Jr.,</p> <p>2 Banner Witcoff, Limited, on behalf of the</p> <p>3 plaintiffs.</p> <p>4 MR. HUGHES: Jim Hughes with Cooley LLP</p> <p>5 on behalf of HyperBranch. And with me today is my</p> <p>6 colleague Adam Pivovar, also with Cooley LLP.</p> <p>7 THE VIDEOGRAPHER: The court reporter,</p> <p>8 Dana Ryan, of DTI Court Reporting Solutions will</p> <p>9 now swear in the witness.</p> <p>10 -----</p> <p>11 DENNIS JAMES RIVET, II, M.D.,</p> <p>12 having been duly sworn, testified as follows:</p> <p>13 -----</p> <p>14 EXAMINATION BY COUNSEL FOR THE DEFENDANT</p> <p>15 BY MR. HUGHES:</p> <p>16 Q Good morning, Dr. --</p> <p>17 A Good morning --</p> <p>18 Q -- Rivet.</p> <p>19 A -- Mr. Hughes.</p> <p>20 Q Could you please state your full name</p> <p>21 for the record?</p> <p>22 A Dennis James Rivet, II.</p>	<p style="text-align: right;">Page 9</p> <p>1 Q And what was the topic of that</p> <p>2 deposition?</p> <p>3 A That was a medical liability, medical</p> <p>4 lawsuit on a patient that I had been involved in.</p> <p>5 Q Okay. And the first time you were</p> <p>6 deposed, when was that?</p> <p>7 A Also -- approximately 2005; also a</p> <p>8 medical lawsuit.</p> <p>9 Q Okay. And that medical lawsuit, what</p> <p>10 type of procedure was involved in the 2005</p> <p>11 lawsuit?</p> <p>12 A Which lawsuit are you asking about?</p> <p>13 Q The 2005 medical liability lawsuit.</p> <p>14 A The 2005 was a -- a shunt procedure, a</p> <p>15 CSF shunting procedure.</p> <p>16 Q And what is a CSF shunt procedure?</p> <p>17 A A procedure where a catheter or device</p> <p>18 is placed to divert spinal fluid from the head</p> <p>19 into another part of the body to facilitate</p> <p>20 drainage in a variety of conditions.</p> <p>21 Q Would you use a dural sealant in that</p> <p>22 type of procedure?</p>

<p style="text-align: right;">Page 10</p> <p>1 A It's possible.</p> <p>2 Q Did you use a dural sealant in that</p> <p>3 type -- in that procedure?</p> <p>4 A I don't recall.</p> <p>5 Q In the 2008 medical liability case you</p> <p>6 mentioned a few minutes ago, what type of</p> <p>7 procedure was involved in that?</p> <p>8 A It was a spinal operation.</p> <p>9 Q What type of spinal operation?</p> <p>10 A As I recall, it was a discectomy -- a</p> <p>11 lumbar discectomy.</p> <p>12 Q And what is a lumbar discectomy?</p> <p>13 A It's surgery where a nerve root or the</p> <p>14 spinal cord is decompressed. Usually removal of a</p> <p>15 small portion of bone and ligament to relieve pain</p> <p>16 or neurological deficit.</p> <p>17 Q And would a surgeon use a dural sealant</p> <p>18 in that type of procedure?</p> <p>19 A It's possible they might, yes.</p> <p>20 Q Did you use a dural sealant in that</p> <p>21 procedure?</p> <p>22 A I don't recall.</p>	<p style="text-align: right;">Page 12</p> <p>1 Q And you mentioned there were multiple</p> <p>2 procedures. What other procedures were involved</p> <p>3 in that 2012 case?</p> <p>4 A My recollection is the patient also had</p> <p>5 a lumbar laminectomy; although, I certainly don't</p> <p>6 recall the specific operation he had.</p> <p>7 Q And what is a lumbar laminectomy?</p> <p>8 A Yeah. Lumbar laminectomy is removal of</p> <p>9 bone and ligaments to decompress the nerve roots</p> <p>10 or spinal cord. Very common neurosurgical</p> <p>11 operation.</p> <p>12 Q In either of these two procedures you</p> <p>13 just mentioned, are dural sealants used in these</p> <p>14 procedures?</p> <p>15 A They may be used in either.</p> <p>16 Q Do you -- did you use a dural sealant</p> <p>17 in either of the procedures?</p> <p>18 A I don't recall the anterior cervical</p> <p>19 discectomy and fusion or the lumbar laminectomy</p> <p>20 whether I used a dural sealant. It certainly</p> <p>21 wasn't an issue in the case.</p> <p>22 Q And in any of these three cases you</p>
<p style="text-align: right;">Page 11</p> <p>1 Q And in the 2008 case, the -- the spinal</p> <p>2 injury on the job, what type of procedure was</p> <p>3 that? Sorry. The 2012 case --</p> <p>4 A Yes, sir.</p> <p>5 Q -- where there was a spinal injury</p> <p>6 on --</p> <p>7 A Yes, sir.</p> <p>8 Q -- the job, what type of procedure was</p> <p>9 that?</p> <p>10 A The patient had multiple procedures.</p> <p>11 Q Do you remember what procedures they</p> <p>12 were?</p> <p>13 A One of the procedures was an anterior</p> <p>14 cervical discectomy and fusion.</p> <p>15 Q And what is that?</p> <p>16 A Where the disks of the cervical spine</p> <p>17 are removed and replaced with either bone graft or</p> <p>18 other materials in order to, again, decompress the</p> <p>19 neural elements, the nerve roots of the spinal</p> <p>20 cord; and then fixation or some sort of construct</p> <p>21 is built to allow for fusion or healing of the</p> <p>22 bone in the area where the disks were removed.</p>	<p style="text-align: right;">Page 13</p> <p>1 just mentioned, were you a defendant in these</p> <p>2 cases?</p> <p>3 A I do not believe I was a defendant --</p> <p>4 the first case I was not --</p> <p>5 Q Okay.</p> <p>6 A -- for sure. And that was -- I was on</p> <p>7 active duty at the time, so -- the prior two</p> <p>8 cases, no, I don't believe I was a named</p> <p>9 defendant.</p> <p>10 Q And in the 2005 case, what was your</p> <p>11 role in your deposition?</p> <p>12 A To discuss my care of the patient as a</p> <p>13 resident physician.</p> <p>14 Q Did you -- was this as a resident</p> <p>15 physician in general, or is it specific to your</p> <p>16 treatment of that patient?</p> <p>17 A My -- the treatment -- my treatment of</p> <p>18 that patient, correct.</p> <p>19 Q And you were not named a defendant in</p> <p>20 that case?</p> <p>21 A That is my recollection. I had no</p> <p>22 follow-up. I believe the case was settled, but</p>

<p style="text-align: right;">Page 14</p> <p>1 I -- I -- I do not think I was a named party to 2 the suit.</p> <p>3 Q And you said you believe the case was 4 settled. That was the outcome of the case?</p> <p>5 A I believe it was, yes. So I had, you 6 know, relocated geographically, and I know of no 7 other -- it never went beyond the deposition, 8 so --</p> <p>9 Q Okay. And where were you located then?</p> <p>10 A I'm sorry?</p> <p>11 Q Where were you located?</p> <p>12 A Oh, during the deposition?</p> <p>13 Q Well, you said you relocated 14 geographically. Where were you located at the 15 time of the deposition?</p> <p>16 A Oh, the deposition was done in 17 St. Louis, Missouri.</p> <p>18 Q Okay. And where was the underlying -- 19 underlying surgery or issue conducted?</p> <p>20 A In St. Louis, Missouri, as well.</p> <p>21 Q Okay. And in the 2008 case, were you a 22 named defendant in that case?</p>	<p style="text-align: right;">Page 16</p> <p>1 Q What --</p> <p>2 A -- so --</p> <p>3 Q What does it mean to be a resident on 4 the procedure?</p> <p>5 A So I scrubbed in the procedure and 6 participating in the surgical procedure but not 7 the attending of record.</p> <p>8 Q So we're -- approximately how many 9 surgeons were involved in the 2008 procedure --</p> <p>10 A The 2000 and?</p> <p>11 Q The 2005 procedure. Pardon me.</p> <p>12 A My recollection is I was involved in 13 one surgical procedure, but I believe the patient 14 had multiple procedures. I -- I don't recall.</p> <p>15 Q In the 2005 case, you mentioned you 16 were a resident, and now you're -- how many 17 surgeons were involved in the procedure that you 18 were a resident conducting?</p> <p>19 A I don't remember.</p> <p>20 Q Okay. And have you ever been sued for 21 malpractice?</p> <p>22 A No.</p>
<p style="text-align: right;">Page 15</p> <p>1 A No, I don't believe I was.</p> <p>2 Q And what was the subject of your 3 deposition testimony in that case?</p> <p>4 A Same thing. The care -- my role in the 5 care of the patient.</p> <p>6 Q Okay. And in the 2008 case, did the 7 case involve a procedure that you performed 8 yourself?</p> <p>9 A I believe I was an assistant on the 10 procedure.</p> <p>11 Q What does that mean, being an assistant 12 on the procedure?</p> <p>13 A Sure. So I was a co-surgeon with a 14 faculty or an attending surgeon during the 15 surgery.</p> <p>16 Q Do you remember your specific role in 17 that surgery?</p> <p>18 A I do not.</p> <p>19 Q And in the 2005 case, did it involve a 20 surgical procedure that you performed?</p> <p>21 A I was a resident on the procedure as 22 well --</p>	<p style="text-align: right;">Page 17</p> <p>1 Q Were either the 2008 or 2005 cases 2 involving malpractice?</p> <p>3 A I believe that's what was alleged.</p> <p>4 Q Who was on those teams?</p> <p>5 A I don't recall.</p> <p>6 Q Were you on the teams involved in the 7 alleged malpractice?</p> <p>8 A So if I understand your question, I do 9 not believe I was named in the lawsuit. I did 10 care for -- I had a role in caring for both of the 11 patients, yes.</p> <p>12 Q In the 2008 procedure, do you remember 13 how many people or entities were named in the 14 lawsuit?</p> <p>15 A I don't.</p> <p>16 Q And in the 2005 procedure, do you know 17 how many people or entities were named in -- as 18 defendants in the case?</p> <p>19 A No, I don't.</p> <p>20 Q So you've been through this before, but 21 let's go over a couple of ground rules so we're on 22 the same page.</p>

Page 18

1 And do you understand that you're here
 2 to testify today and you're sworn in under oath to
 3 tell the truth just like you're before a judge and
 4 a jury?
 5 Do you understand that?
 6 A Yes.
 7 Q And I'm going to ask you a number of
 8 questions today. If any of my questions are
 9 unclear, please let me know so I can clarify the
 10 question for you.
 11 Do you understand that?
 12 A Yes.
 13 Q And during the day, your counsel may
 14 object, but unless he instructs you not to answer,
 15 you still need to answer the question.
 16 Do you understand that?
 17 A Yes.
 18 Q And there's a court reporter here
 19 taking down everything we say, so it's important
 20 we don't talk over each other. We let one person
 21 finish their answer or question before we speak.
 22 Do you understand that?

Page 19

1 A Yes.
 2 Q And because she's taking down
 3 everything in stenography, you need to have verbal
 4 answers; head nods and shakes of the head are
 5 inappropriate.
 6 Do you understand that?
 7 A Yes.
 8 Q And throughout the day if you need a
 9 break, let me know. We'll probably take one every
 10 hour or so. And if you need a break, let me know,
 11 as I said; but if there's an open question, I'll
 12 ask that you answer that question prior to the
 13 break.
 14 Do you understand that?
 15 A Yes.
 16 Q And do you understand these rules as
 17 I've laid them out?
 18 A Yes, I do.
 19 Q Is there any reason why you cannot give
 20 your best and truthful testimony today?
 21 A No.
 22 Q Okay. No medications or other

Page 20

1 circumstances?
 2 A Correct.
 3 Q And you understand you're here to
 4 testify regarding two expert reports that you
 5 submitted in this litigation; is that correct?
 6 A Yes.
 7 Q And when were you retained as an expert
 8 in this case?
 9 A I don't recall the exact date.
 10 Q Was it before July of 2017?
 11 A I don't recall the exact date. It
 12 could have been.
 13 Q Was -- do you remember when you first
 14 had contact with anyone from the Banner Witcoff
 15 firm?
 16 A I don't recall the exact day, no.
 17 Q Approximately?
 18 A Sometime in -- I believe it was the
 19 spring of 2017.
 20 Q And were you retained approximately in
 21 the spring of 2017 for this case?
 22 A I believe that's when it was.

Page 21

1 Certainly that's something I could find out.
 2 Q And do you know how you were identified
 3 as a potential expert witness in this case?
 4 A I don't.
 5 Q In the spring of 2017 when someone from
 6 the Banner Witcoff firm first contacted you, do
 7 you remember who it was?
 8 A I believe it was Christopher Roth.
 9 Q Do you remember how they contacted you?
 10 A Or it might have been the
 11 administrative assistant for Christopher Roth,
 12 but . . .
 13 Email. I believe I received an email.
 14 Q And did you follow up on that email?
 15 A Yes, I think that's what facilitated
 16 our phone conversation.
 17 Q And approximately how long after that
 18 phone conversation were you retained as an expert
 19 witness?
 20 A I think it was in the next two to four
 21 weeks.
 22 Q Okay. Did Christopher Roth -- Roth say

<p style="text-align: right;">Page 22</p> <p>1 then why he emailed you?</p> <p>2 A Yes. I believe the email was that he</p> <p>3 wanted to speak about my potential involvement in</p> <p>4 a -- in a case.</p> <p>5 Q Did -- before you were retained, did he</p> <p>6 ever identify to you how he got your name as a</p> <p>7 potential expert witness?</p> <p>8 A I do not believe Mr. Roth did.</p> <p>9 Q Did anyone else convey to you how they</p> <p>10 got your name as a potential expert witness?</p> <p>11 A Did anyone else convey to me how they</p> <p>12 got my name?</p> <p>13 Q Yeah. Did anyone else -- strike that.</p> <p>14 Did anyone else convey to you how you</p> <p>15 were identified as a potential expert witness?</p> <p>16 A I was contacted by a firm who emailed</p> <p>17 me and asked my permission, I believe, to forward</p> <p>18 my name and contact information to a firm. And I</p> <p>19 don't remember if they identified Banner Witcoff</p> <p>20 so I assume -- although I don't know for sure --</p> <p>21 that they forwarded that to Banner Witcoff.</p> <p>22 Q So you just mentioned firm twice. And</p>	<p style="text-align: right;">Page 24</p> <p>1 Q Have you ever been retained through any</p> <p>2 other expert witness firms?</p> <p>3 A I do not believe so, no.</p> <p>4 Q Have you ever been as a potential</p> <p>5 candidate for retention with any other expert</p> <p>6 witness firms?</p> <p>7 A Absolutely.</p> <p>8 Q Okay.</p> <p>9 A That -- I received, I would describe,</p> <p>10 multiple requests and routinely receive them from</p> <p>11 expert witness firms. That's why I asked "working</p> <p>12 with," so --</p> <p>13 Q So is the --</p> <p>14 A I've communicated with them, certainly,</p> <p>15 but I wouldn't describe that as working with them.</p> <p>16 So I --</p> <p>17 Q Had --</p> <p>18 A -- don't believe I've ever been</p> <p>19 retained by any other firm.</p> <p>20 Q Well, I think the question is not</p> <p>21 retained by the expert witness firm but retained</p> <p>22 through them with another --</p>
<p style="text-align: right;">Page 23</p> <p>1 the first time you were contacted by a firm, would</p> <p>2 that be an expert witness consulting firm?</p> <p>3 A Yes.</p> <p>4 Q And the second time you mentioned a</p> <p>5 firm there, you're referring --</p> <p>6 A Banner Wit- --</p> <p>7 Q -- a potential law firm?</p> <p>8 A Excuse me.</p> <p>9 Banner Witcoff, yes. Yeah.</p> <p>10 Q And have you worked with -- which</p> <p>11 expert witness consulting firm was that that</p> <p>12 contacted you?</p> <p>13 A I believe it was Elite.</p> <p>14 Q Have you worked with Elite before?</p> <p>15 A Yes.</p> <p>16 Q When did you work with Elite before?</p> <p>17 A I -- I don't know the exact dates.</p> <p>18 I've worked with them on, I believe, two cases, in</p> <p>19 2016 and '17.</p> <p>20 Q Have you ever worked with any other</p> <p>21 expert witness firms?</p> <p>22 A Can you define "worked with"?</p>	<p style="text-align: right;">Page 25</p> <p>1 A Agreed. Either by them or through</p> <p>2 them, yeah.</p> <p>3 Q So the only time you've ever been</p> <p>4 retained for an expert -- take a step back.</p> <p>5 Does that also cover consulting</p> <p>6 engagements or just expert witness engagements?</p> <p>7 A I -- I'm not sure the definition of</p> <p>8 "consulting," so in -- in our university,</p> <p>9 consulting is defined as any outside work. So</p> <p>10 consulting includes work unrelated to medical</p> <p>11 expert witness testimony at all, so --</p> <p>12 And have I been contacted or referred</p> <p>13 regarding consulting? Yes.</p> <p>14 Q Is what you're doing here in this case</p> <p>15 considered consulting by your university?</p> <p>16 A It is considered outside professional</p> <p>17 activity, yes.</p> <p>18 Q And that's the same as -- just so we</p> <p>19 use the same terms, is that the same as</p> <p>20 consulting for --</p> <p>21 A I believe it is, yes. I don't think</p> <p>22 they differentiate the two.</p>

<p style="text-align: right;">Page 26</p> <p>1 Q Okay. I'm not trying to pin you down</p> <p>2 on the legal meaning of a term. I'm just trying</p> <p>3 to get the terminology so we can have this</p> <p>4 discussion on the same page here.</p> <p>5 A Sure.</p> <p>6 There's -- there are clearly outside</p> <p>7 professional activities that are consulting that</p> <p>8 are unrelated to medical ex- -- expert witness</p> <p>9 work that I have performed, and I've also been</p> <p>10 contacted about the possibility of performing and</p> <p>11 then not done, so . . .</p> <p>12 Q So with this expert witness, you mean</p> <p>13 regarding litigations?</p> <p>14 A Correct. Or even prior to a litigation</p> <p>15 stage; sometimes it isn't necessarily litigation.</p> <p>16 Q But it might mature into a litigation?</p> <p>17 A Not always.</p> <p>18 Q Okay. And approximately how much time</p> <p>19 do you spend in outside consulting?</p> <p>20 A Not much.</p> <p>21 Q Approximately what percent of your, you</p> <p>22 know, working days per year do you spend --</p>	<p style="text-align: right;">Page 28</p> <p>1 but may have involved the qualifications of the</p> <p>2 surgeon for credentialing purposes, for example.</p> <p>3 Q Any other examples of consulting?</p> <p>4 A One other example that falls under our</p> <p>5 university's definition is teaching, so teaching</p> <p>6 on the use of medical devices to industry either</p> <p>7 clinical representatives or sales representatives</p> <p>8 that I have experience in using.</p> <p>9 Q And any other examples of consulting?</p> <p>10 A If we -- another example would be if we</p> <p>11 speak at an event that is not -- that continuing</p> <p>12 medical education, nursing education is not</p> <p>13 provided, then that counts as outside consulting.</p> <p>14 So if we're going to present on any topic to an</p> <p>15 audience that doesn't involve the provision of</p> <p>16 medical education formally for that talk or</p> <p>17 presentation, then it's considered consulting, and</p> <p>18 I've done that.</p> <p>19 Q But if there is a continuing education</p> <p>20 component, that's not considered consulting?</p> <p>21 A That's correct.</p> <p>22 Q And any other examples of consulting</p>
<p style="text-align: right;">Page 27</p> <p>1 A Sure.</p> <p>2 Q -- on outside consulting?</p> <p>3 A I would estimate less than 2 percent.</p> <p>4 Q So less than 2 percent of your time in</p> <p>5 a given year is done --</p> <p>6 A Correct.</p> <p>7 Q And so we're clear, "consulting" is the</p> <p>8 broad term of litigation work or other outside</p> <p>9 professional activities from your university?</p> <p>10 A Correct.</p> <p>11 Q And other than the potential litigation</p> <p>12 consulting, what is the subject matter of the</p> <p>13 consulting that you engage in?</p> <p>14 A So it's involved, for example, being on</p> <p>15 a medical advisory board to an industry company</p> <p>16 who is developing technology -- is one example</p> <p>17 recently that I did.</p> <p>18 Q Okay. What are other examples?</p> <p>19 A Other examples are I was retained by</p> <p>20 the Navy to review a surgeon's performance as a --</p> <p>21 a neutral outside party. So it involved review of</p> <p>22 records that certainly wouldn't lead to litigation</p>	<p style="text-align: right;">Page 29</p> <p>1 work --</p> <p>2 A Not that I can --</p> <p>3 Q -- you've --</p> <p>4 A -- think of.</p> <p>5 Q -- conducted?</p> <p>6 And for how many years have you been</p> <p>7 spending approximately 2 percent of your time</p> <p>8 doing consulting work?</p> <p>9 A Less than three.</p> <p>10 Q And you mentioned a medical advisory</p> <p>11 board.</p> <p>12 A Can I --</p> <p>13 Q Sure.</p> <p>14 A Can I clarify one thing?</p> <p>15 I have done consulting prior to three</p> <p>16 years ago that was not under -- that -- that the</p> <p>17 definition of consulting -- I didn't work for the</p> <p>18 same university, so -- but it -- it represented</p> <p>19 even less than 2 -- you know, I would say it's</p> <p>20 less than a half of a percent of my time prior to</p> <p>21 that. Between 2003 and 2014, so ten years prior</p> <p>22 to that, a smaller percentage.</p>

<p style="text-align: right;">Page 30</p> <p>1 Q Okay. So I'm going to ask a couple of</p> <p>2 follow-on questions, but for time frame let's look</p> <p>3 at 2003 to the present.</p> <p>4 A Sure.</p> <p>5 Q And you mentioned medical advisory</p> <p>6 boards before, teaching devices at medical --</p> <p>7 various uses of medical devices, talks to</p> <p>8 conferences where no continuing education was</p> <p>9 involved --</p> <p>10 A That's right.</p> <p>11 Q -- and the -- the fourth category was</p> <p>12 speaking at conference or presentations where</p> <p>13 medical education was involved.</p> <p>14 A Okay.</p> <p>15 Q And in those areas, have you ever</p> <p>16 consulted regarding dural sealants?</p> <p>17 A No, I don't believe I have.</p> <p>18 Q Have you ever consulted regarding fiber</p> <p>19 and glue?</p> <p>20 A No, I don't believe so.</p> <p>21 Q Have you ever consulted regarding any</p> <p>22 product that a surgeon may use as a replacement as</p>	<p style="text-align: right;">Page 32</p> <p>1 A -- prior --</p> <p>2 Q -- this case to --</p> <p>3 A Yes. Okay. Just clarifying that.</p> <p>4 Q And before this case, have you ever had</p> <p>5 a consulting or other engagement with any Integra</p> <p>6 entity?</p> <p>7 A Not that I'm aware of.</p> <p>8 Q And when I say "Integra entity," I mean</p> <p>9 Integra LifeSciences, Integra LifeSciences Sales,</p> <p>10 or other related entities that you're aware of.</p> <p>11 A Understood. And I believe the answer</p> <p>12 is, no, I'm not aware of any consulting</p> <p>13 relationship with an Integra or Integra affiliate.</p> <p>14 Q Okay. And the same question for</p> <p>15 Confluent Surgical, Incorporated.</p> <p>16 A Same answer. I'm not aware of any</p> <p>17 prior consulting with that entity.</p> <p>18 Q And the same question for Incept LLC.</p> <p>19 A Agreed. The same answer.</p> <p>20 Q And same question for HyperBranch</p> <p>21 Medical Technology.</p> <p>22 A Same. No prior consulting that I'm</p>
<p style="text-align: right;">Page 31</p> <p>1 a dural sealant in an operation?</p> <p>2 MR. ALTHERR: Object to the form.</p> <p>3 THE WITNESS: Not that I'm aware of.</p> <p>4 BY MR. HUGHES:</p> <p>5 Q Have you ever worked with Integra</p> <p>6 LifeSciences before?</p> <p>7 A Can I just go back --</p> <p>8 Q Sure.</p> <p>9 A -- to your last question?</p> <p>10 I assume you're excepting the current</p> <p>11 case.</p> <p>12 Q Yes, yes.</p> <p>13 A Okay.</p> <p>14 Q Yeah.</p> <p>15 A Because obviously the answer would be</p> <p>16 yes. Right now, as I've established, I'm here</p> <p>17 consultant basis and --</p> <p>18 Q Yeah. Of course. I'm -- I'm trying --</p> <p>19 A Making --</p> <p>20 Q -- to --</p> <p>21 A -- sure --</p> <p>22 Q -- get before --</p>	<p style="text-align: right;">Page 33</p> <p>1 aware of.</p> <p>2 Q Okay. Do you know who -- so you're</p> <p>3 familiar with the Integra dural sealant product;</p> <p>4 correct?</p> <p>5 A Yes.</p> <p>6 Q Do you know who your local sales rep is</p> <p>7 for the Integra dural sealant product?</p> <p>8 A I would recognize him, but I can't</p> <p>9 recall his name.</p> <p>10 Q Do you know -- do you have more than</p> <p>11 one sales representative?</p> <p>12 A It's possibly we do, yes.</p> <p>13 Q For the Integra dural sealant product?</p> <p>14 A Yes, it's very possible we have more</p> <p>15 than one.</p> <p>16 Q Do you know approximately how many?</p> <p>17 A I don't.</p> <p>18 Q Now, did you have any discussions with</p> <p>19 the Integra representative about your role in this</p> <p>20 case?</p> <p>21 A No.</p> <p>22 Q Do you know if the Integra</p>

<p style="text-align: right;">Page 34</p> <p>1 representative is aware of your role in this case?</p> <p>2 A I do not.</p> <p>3 Q And I think I asked this, but in case I</p> <p>4 didn't, the various consulting engagements, have</p> <p>5 you ever consulted in a dural sealant before?</p> <p>6 A I agree. I believe you asked it, and</p> <p>7 the answer is no.</p> <p>8 Q Okay. You mentioned the Elite</p> <p>9 consulting firm?</p> <p>10 A Yes.</p> <p>11 Q And I believe it was 2016 and 2017 you</p> <p>12 mentioned that you had worked in some capacity</p> <p>13 with Elite?</p> <p>14 A Yes.</p> <p>15 Q And in 2016, what capacity did you work</p> <p>16 with Elite?</p> <p>17 A I believe that Elite was -- similar to</p> <p>18 this case, they had contacted me and asked could</p> <p>19 they forward my information to a legal firm</p> <p>20 regarding a -- a medical case.</p> <p>21 Q Do you know approximately how many</p> <p>22 times in 2016 they contacted you?</p>	<p style="text-align: right;">Page 36</p> <p>1 A Correct.</p> <p>2 Q And what engagements were you retained</p> <p>3 through or -- or -- or -- you know, worked through</p> <p>4 Elite with in 2016?</p> <p>5 A I think there were a few medical-legal</p> <p>6 cases that they referred a law firm that then</p> <p>7 contacted me to review medical records on a case.</p> <p>8 Q And how many cases were there?</p> <p>9 A One or two cases. I don't recall the</p> <p>10 exact number.</p> <p>11 Q And let me take a step back.</p> <p>12 When I say "case," I meant how many</p> <p>13 different consulting engagements did you partake</p> <p>14 in?</p> <p>15 A One or two.</p> <p>16 Q Okay.</p> <p>17 A Yeah.</p> <p>18 Q Because my understanding is sometimes</p> <p>19 surgeons refer to a case as an individual case in</p> <p>20 theater?</p> <p>21 A Understood. I was using the legal</p> <p>22 sense.</p>
<p style="text-align: right;">Page 35</p> <p>1 A One or two times.</p> <p>2 Q Do you know if any of those cases</p> <p>3 involved dural sealants?</p> <p>4 A I don't know of another case that</p> <p>5 involved dural sealants, but certainly they could</p> <p>6 have. For example, I didn't -- many of the cases</p> <p>7 I didn't see the exact operative reports or</p> <p>8 details that I would be able to say that with</p> <p>9 certainty.</p> <p>10 Q And were -- did you ever engage in any</p> <p>11 consulting activities in your relation -- or</p> <p>12 through Elite in 2016 -- that you were first</p> <p>13 contacted by them in 2016?</p> <p>14 A Yes.</p> <p>15 Q And which -- which engagements were --</p> <p>16 did you partake in?</p> <p>17 A I'm not sure I understand what</p> <p>18 you're --</p> <p>19 Q Yeah. Strike that.</p> <p>20 So in 2016, you were retained or</p> <p>21 engaged in consulting agreements through Elite;</p> <p>22 correct?</p>	<p style="text-align: right;">Page 37</p> <p>1 Q Okay. Thank you. Just clarifying the</p> <p>2 terms back and forth.</p> <p>3 A (Witness nods head.)</p> <p>4 Q And were any of these patent litigation</p> <p>5 cases?</p> <p>6 A Patent litigation is what you --</p> <p>7 Q (Indicated affirmative.)</p> <p>8 A No, they were not.</p> <p>9 Q And none of them involved dural</p> <p>10 sealants?</p> <p>11 A Not that I'm aware of.</p> <p>12 Q And same set of questions for 2017.</p> <p>13 Approximately how -- how many times were you</p> <p>14 contacted by Elite for a potential engagement in</p> <p>15 2017?</p> <p>16 A One or two times.</p> <p>17 Q Including --</p> <p>18 A And I'm including this case.</p> <p>19 Q Okay. And other than this case, were</p> <p>20 there any other cases that you signed an</p> <p>21 engagement agreement in?</p> <p>22 A I guess -- "engagement agreement," I</p>

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1 agreed to work with a separate firm -- a separate
 2 legal firm that I was originally referred to -- or
 3 referred by Elite, and so I agree to -- if
 4 that's -- if that's an engagement, then, yes.
 5 **Q And that's other than this case that --**
 6 A That's correct, yes.
 7 **Q And was that a medical malpractice**
 8 **case?**
 9 A Yes, sir, it was.
 10 **Q And were there any other patent**
 11 **litigation cases?**
 12 A No.
 13 **Q Is this the first patent litigation**
 14 **case that you've been retained to consult with?**
 15 A Yes.
 16 **Q When was -- so going back to your**
 17 **discussion with the Banner Witcoff firm in the**
 18 **spring of 2017, did you speak with anyone else**
 19 **from Banner & Witcoff at that time?**
 20 A What time do you refer to?
 21 **Q Spring of 2017.**
 22 A So, yes. So during the spring of 2017,

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1 I've spoken with, I believe, an administrative
 2 assistant from the firm as well as Mr. Altherr was
 3 present.
 4 **Q Anyone else associated with the**
 5 **Banner & Witcoff firm?**
 6 A I communicated via email with a
 7 paralegal, but I don't -- I don't think I spoke
 8 with anyone else.
 9 **Q And approximately how many times did**
 10 **you meet with them or speak with them?**
 11 A I've met with Mr. Altherr on one prior
 12 occasion, and I can't recall how many
 13 conversations we've had off the top of my head.
 14 Certainly I feel comfortable saying more than ten.
 15 **Q And you say you've met with Mr. Altherr**
 16 **one prior occasion. Do you mean one prior**
 17 **occasion before this deposition today?**
 18 A Correct.
 19 **Q And did you meet with Mr. Altherr in**
 20 **preparation for this deposition today?**
 21 A Yes.
 22 **Q And approximately how long did you meet**

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1 **with Mr. Altherr for?**
 2 A Six hours.
 3 **Q When was that?**
 4 A Yesterday.
 5 **Q And did you speak with him on the phone**
 6 **regarding this deposition prior to that?**
 7 A Yes.
 8 **Q Approximately how many times?**
 9 A I think we probably discussed the
 10 deposition only one or two prior times.
 11 **Q Did you have any conversations other**
 12 **than scheduling conversations regarding this**
 13 **deposition?**
 14 A No.
 15 **Q Did you meet with anyone else in**
 16 **preparation for this deposition?**
 17 A No.
 18 **Q Did you speak with anyone else in**
 19 **preparation for this deposition?**
 20 A I spoke with Mr. Roth.
 21 **Q Okay. Did you speak with anyone**
 22 **associated with any of the plaintiffs in this firm**

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1 **other than the Banner & Witcoff firm in**
 2 **preparation for this deposition?**
 3 A And can you define -- the last several
 4 questions you've asked, you've asked "in
 5 preparation for this deposition."
 6 Can you define what you mean by "in
 7 preparation for the deposition."
 8 **Q A little later we'll get into potential**
 9 **discussions with Dr. Mays or anyone else.**
 10 A Okay.
 11 **Q I'm referring now to legal counsel.**
 12 **So did you speak with anyone else from**
 13 **Banner & Witcoff or other legal counsel in**
 14 **preparation for the deposition?**
 15 A No, I've only spoken to Mr. Roth and
 16 Mr. Altherr.
 17 **Q Okay.**
 18 A The reason I said the last thing was I
 19 believe one could construe any conversation that I
 20 had with anyone regarding this case was in
 21 preparation for this deposition, so if your
 22 questions were related to that, then I need to

<p style="text-align: right;">Page 42</p> <p>1 expand how many people I spoke to.</p> <p>2 Q No. Fair enough. I think -- I'll</p> <p>3 clarify, referring in the last week or two or</p> <p>4 three --</p> <p>5 A Sure.</p> <p>6 Q -- in focusing on what's going to be</p> <p>7 occurring today.</p> <p>8 A Understood.</p> <p>9 Q So do you have anything to correct</p> <p>10 based on --</p> <p>11 A I don't --</p> <p>12 Q -- that understanding?</p> <p>13 A -- no.</p> <p>14 Q And did you speak with anyone at any of</p> <p>15 the Integra entities in preparation for your</p> <p>16 deposition today?</p> <p>17 A No.</p> <p>18 Q Do you know if your Integra sales rep</p> <p>19 is aware of your deposition today?</p> <p>20 A I do not.</p> <p>21 Q Do you know if he's --</p> <p>22 A I'm not aware I should say.</p>	<p style="text-align: right;">Page 44</p> <p>1 Q And what were the outlines of the case</p> <p>2 that you discussed with Mr. Roth?</p> <p>3 A That there were --</p> <p>4 MR. ALTHERR: All right. I'm going to</p> <p>5 caution the witness at this time. You can discuss</p> <p>6 anything up until the time you were engaged to be</p> <p>7 an expert.</p> <p>8 All right. Once he's engaged, I'm</p> <p>9 going to assert a work product privilege.</p> <p>10 THE WITNESS: Sure.</p> <p>11 He asked me some of the questions you</p> <p>12 asked -- you asked today, what my prior, you know,</p> <p>13 deposition and malpractice and/or legal consulting</p> <p>14 background was, and what -- what might be the</p> <p>15 nature of my involvement. If I were to be</p> <p>16 retained, what it would involve.</p> <p>17 We talked about the time frame, my</p> <p>18 schedule. Was I able to commit from a -- from a</p> <p>19 time perspective, et cetera.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q Approximately how much time did he</p> <p>22 indicate to you that this engagement would take</p>
<p style="text-align: right;">Page 43</p> <p>1 Q Do you know if he's aware you're being</p> <p>2 deposed in this case?</p> <p>3 A I'm not aware.</p> <p>4 Q And did you speak with anyone from</p> <p>5 Confluent Surgical or Incept LLC in preparation</p> <p>6 for your deposition today?</p> <p>7 A No.</p> <p>8 Q Okay.</p> <p>9 A Again, I think I'd go back to say if</p> <p>10 you mean in the last two or three weeks have I</p> <p>11 spoken with anyone from HyperBranch or Integra,</p> <p>12 the answer is no.</p> <p>13 Q Okay. And we can get to other</p> <p>14 interactions --</p> <p>15 A Yeah.</p> <p>16 Q -- with --</p> <p>17 A I just want to make sure that I'm clear</p> <p>18 when I -- when I answer.</p> <p>19 Q When you first had a conversation with</p> <p>20 Mr. Roth in this case around the spring of 2017,</p> <p>21 what did you discuss?</p> <p>22 A The outlines of the case.</p>	<p style="text-align: right;">Page 45</p> <p>1 from you -- for you?</p> <p>2 A I don't think we discussed how much</p> <p>3 time it would require. We discussed the timing;</p> <p>4 i.e., I explained if this was something that</p> <p>5 required multiple meetings in the next two months,</p> <p>6 I would be unable to commit to that sort of thing,</p> <p>7 that sort of timing meaning what was the time</p> <p>8 frame that the case might occur over.</p> <p>9 What I would describe as vetting me:</p> <p>10 was I an appropriate person and could I commit to</p> <p>11 the job.</p> <p>12 Q Did he ask if you'd ever used the</p> <p>13 DuraSeal product?</p> <p>14 A I don't recall if he asked that.</p> <p>15 Q Did he ask if you'd ever used the</p> <p>16 HyperBranch Adherus product?</p> <p>17 A I don't recall if he asked that.</p> <p>18 Q Do you recall discussing your use of</p> <p>19 the DuraSeal product with Mr. Roth before you were</p> <p>20 engaged?</p> <p>21 A No.</p> <p>22 Q And before you were engaged in this</p>

<p style="text-align: right;">Page 46</p> <p>1 case, do you remember discussing the HyperBranch</p> <p>2 Adherus product with Mr. Roth?</p> <p>3 A No.</p> <p>4 Q So same questions for anyone associated</p> <p>5 with the Barren Witcoff firm. Before you were</p> <p>6 engaged, did you discuss your use of the DuraSeal</p> <p>7 product?</p> <p>8 A No.</p> <p>9 Q Same question. Before you were</p> <p>10 engaged, did you discuss with anyone associated</p> <p>11 with Banner & Witcoff about your use of the</p> <p>12 Adherus product?</p> <p>13 A No.</p> <p>14 Q When you were discussing with Elite,</p> <p>15 did you discuss with Elite your use of the dural</p> <p>16 sealant [verbatim] product?</p> <p>17 A No.</p> <p>18 Q Did you discuss with Elite or anyone</p> <p>19 associated with Elite the use of the HyperBranch</p> <p>20 Adherus product?</p> <p>21 A I don't think I had any discussions</p> <p>22 with Elite. I think our communications were via</p>	<p style="text-align: right;">Page 48</p> <p>1 Q When you were discussing a potential</p> <p>2 engagement for Elite, did you discuss your use of</p> <p>3 dural sealants in general?</p> <p>4 A No. Again, I don't think I had any</p> <p>5 discussion with Elite. I think our communication</p> <p>6 was solely via email.</p> <p>7 Q Okay. And in those email</p> <p>8 communications, if you want to include email</p> <p>9 communications in discussions --</p> <p>10 A Okay.</p> <p>11 Q -- did you --</p> <p>12 A Yeah.</p> <p>13 Q -- discuss dural sealants in general at</p> <p>14 all with anyone from Elite?</p> <p>15 A Not that I recall.</p> <p>16 Q And, again, for the rest of today,</p> <p>17 unless it matters from your perspective, if --</p> <p>18 when I say discussions or conversations, I'm going</p> <p>19 to refer to email communication being the same as</p> <p>20 a voice conversation.</p> <p>21 A Great. I understand now.</p> <p>22 Q Okay. And did you discuss with anyone</p>
<p style="text-align: right;">Page 47</p> <p>1 email.</p> <p>2 Q Prior to being engaged in this</p> <p>3 litigation, did you have any discussion with</p> <p>4 anyone regarding your use of the dural sealant</p> <p>5 [verbatim] product?</p> <p>6 A Would you repeat the question?</p> <p>7 Q Prior to being engaged in this</p> <p>8 litigation, did you have any discussion with</p> <p>9 anyone regarding your use of the dural sealant</p> <p>10 [verbatim] product in relation to what you're</p> <p>11 testifying on in this litigation?</p> <p>12 MR. ALTHERR: Object to the form.</p> <p>13 THE WITNESS: The question you're</p> <p>14 asking is prior to engagement, if I understand it,</p> <p>15 have I had a discussion about dural sealants. You</p> <p>16 didn't express a sealant.</p> <p>17 Absolutely.</p> <p>18 BY MR. HUGHES:</p> <p>19 Q So the last question I meant DuraSeal,</p> <p>20 the Integra DuraSeal product.</p> <p>21 A Have I ever discussed DuraSeal, the</p> <p>22 Integra product? Yes.</p>	<p style="text-align: right;">Page 49</p> <p>1 associated with the Banner & Witcoff firm dural</p> <p>2 sealants in general prior to being retained in</p> <p>3 this case?</p> <p>4 A Not that I recall.</p> <p>5 Q Prior to being engaged in this case, is</p> <p>6 it correct that you never discussed dural sealants</p> <p>7 with the -- anyone from the Banner & Witcoff firm?</p> <p>8 A I believe that's correct. I mean, I</p> <p>9 guess one could construe that when he mentioned a</p> <p>10 case between two companies, it's -- it's fair to</p> <p>11 say I was aware that the one company, that's their</p> <p>12 primary product. So I knew the case would involve</p> <p>13 that, and our discussions involved companies that</p> <p>14 make dural sealants.</p> <p>15 Did we have discussions regarding the</p> <p>16 specifics of dural sealants prior to engagement?</p> <p>17 No.</p> <p>18 Our discussion really revolved around</p> <p>19 the logistics of my involvement, my background, my</p> <p>20 experience, what -- what my clinical practice</p> <p>21 was -- involved; maybe a paraphrase, my</p> <p>22 credentials and my ability to perform the work</p>

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1 from a time perspective.

2 **Q You mentioned you discussed companies**

3 **that make dural sealants or involved with dural**

4 **sealants in those discussions prior to being**

5 **retained in this case.**

6 **Did you discuss any other companies**

7 **other than the named defendants and plaintiff in**

8 **this litigation?**

9 A No.

10 **Q When was the first time that you became**

11 **aware of the Integra DuraSeal product?**

12 A I -- I -- that would be hard for me to

13 give you an exact date. Years ago.

14 **Q Do you know approximately when it was?**

15 A I would guess around 2000. Sometime

16 during my training, so sometime between 1998 and

17 2002.

18 **Q Do you recall how you first became**

19 **aware of the DuraSeal product?**

20 A It -- basically it was used clinically.

21 It -- it was -- in a way that we've become

22 familiar with many products, it was discussed at

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1 national meetings; it was demonstrated to us by

2 representatives of the company. And we began to

3 use it clinically.

4 **Q Do you know whether or not this was**

5 **post-FDA approval of the DuraSeal product?**

6 A I -- I do not.

7 **Q Were you involved in any clinical**

8 **studies associated with the DuraSeal product?**

9 A Not that I'm aware of.

10 **Q And have you ever been involved in any**

11 **clinical study regarding DuraSeal -- the DuraSeal**

12 **product?**

13 A Not that I'm aware of.

14 **Q And are you aware that there is a**

15 **DuraSeal product and a DuraSeal Xact product?**

16 A Yes.

17 **Q And my questions I just said are**

18 **referring to DuraSeal and DuraSeal Xact product.**

19 A Understood. And, yes, I'm aware of

20 both of those.

21 **Q And do you have any change of your**

22 **testimony you just gave based on that**

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1 **understanding?**

2 A Maybe you can --

3 **Q Meaning --**

4 A Not that I'm --

5 **Q -- were you --**

6 A -- aware --

7 **Q -- involved --**

8 A -- of.

9 **Q -- in any clinical studies of the**

10 **DuraSeal --**

11 A Oh --

12 **Q -- or DuraSeal Xact product?**

13 A -- thank you for clarifying.

14 I am not aware of being involved in any

15 clinical trials involving either the DuraSeal or

16 DuraSeal Xact.

17 When I say "I am not aware," I'll

18 clarify by saying it's possible that a faculty

19 member in my department was involved and I wasn't

20 aware of it, and I worked with that faculty

21 member. So it's possible that the department I

22 was a member of was participating in a trial that

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1 I was completely unaware of as a resident --

2 **Q Understood.**

3 A -- so --

4 **Q Understood.**

5 **Is it fair to say that when you first**

6 **became aware of the DuraSeal product that it was**

7 **after FDA approval?**

8 A That is the most likely, yes.

9 **Q So then it's also fair to say that the**

10 **first time you used the DuraSeal product was after**

11 **FDA approval?**

12 A I agree. Because if I was using it

13 prior to FDA approval, I would have assumed it

14 would be under a trial basis only.

15 **Q Okay.**

16 A But as I can't recall the exact date,

17 can I say that with 100 percent certainty? No, I

18 can't.

19 **Q And do you know when -- do you know who**

20 **manufactured the DuraSeal product around the time**

21 **you first became aware of it?**

22 A I do not.

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1 Q Do you know when the DuraSeal product
2 became an Integra product?
3 A No, I do not.
4 Q Approximately how many times have you
5 used the DuraSeal product?
6 A Yeah, it's a -- it's an estimate, and I
7 think it's in my expert report. If I could have
8 that in front of me while I'm answering the
9 question, that would be great.
10 Q We -- we can follow up with that --
11 A Okay.
12 Q -- a little bit later.
13 A So --
14 Q Do you have -- without the --
15 A -- hundreds.
16 Q Hundreds?
17 A Hundreds of times, yes.
18 Q Okay. Would it -- is it fair to say
19 more than a thousand times?
20 A I don't think that's fair, no.
21 Q And have you used the DuraSeal Xact
22 product?

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1 A Yes.
2 Q What percentage of -- well, I'll take a
3 step back.
4 Approximately how many times have you
5 used the DuraSeal Xact product?
6 A Again, an estimate, I'd feel over a
7 hundred.
8 Q Okay. And in your history of using
9 either of the DuraSeal products, what is the
10 approximate percentage of your use of DuraSeal
11 versus DuraSeal Xact?
12 A I would estimate -- it is weighted
13 towards the DuraSeal, and I'm going to estimate
14 two-thirds DuraSeal -- or 70 percent DuraSeal,
15 30 percent DuraSeal Xact is an estimate.
16 Q Do you know when DuraSeal Xact became
17 available to surgeons?
18 A I do not. I certainly recall the
19 discussion of it.
20 Q Is it your understanding that the
21 DuraSeal Xact product became available to surgeons
22 after the DuraSeal product?

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1 A That is my recollection, yes.
2 Q Okay. And for the DuraSeal product,
3 apart from the DuraSeal Xact product, do you use
4 the DuraSeal product in craniotomies?
5 A Yes.
6 Q Do you use the DuraSeal product in
7 spinal surgeries?
8 A Again, DuraSeal Xact or DuraSeal?
9 Q The DuraSeal.
10 A Maybe for clarity we can say DuraSeal
11 and just say Xact? Would that make it easier for
12 both of us?
13 We can say DuraSeal to mean the
14 DuraSeal, and we can say Xact to mean the DuraSeal
15 Xact. Is that --
16 Q For this --
17 A -- acceptable?
18 Q For this next series of questions, yes.
19 Later on I might combine them altogether.
20 A Sure.
21 Q For these, let's -- that's a good
22 point.

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1 So the DuraSeal product -- have you
2 used the DuraSeal product in craniotomies?
3 A Yes.
4 Q Have you used the DuraSeal product in
5 spinal surgeries?
6 A Yes, I believe I have.
7 Q Have you used the Xact product in
8 craniotomies?
9 A Not that I'm aware of.
10 Q Have you used the Xact product in
11 spinal surgeries?
12 A Yes.
13 Q Of craniotomies, approximately what
14 percent -- let's take a step back.
15 When I say "craniotomies," I'm
16 referring to any --
17 A Cranial operation?
18 Q Cranial operation, yes.
19 A Okay.
20 Q Just so we're on the same page. There
21 might be more nuances in type of operations that
22 are remaining, but gen- -- cranial operations.

<p style="text-align: right;">Page 58</p> <p>1 In what percent of the cranial 2 operations you've performed have you used DuraSeal 3 on? 4 A The majority. 5 Q The majority. 6 A Meaning if I used a dural sealant 7 product, the majority of them I use DuraSeal, not 8 the Xact product. But I didn't mean -- the 9 majority of craniotomies, I use a dural sealant. 10 Most craniotomies do not require. 11 Q Okay. 12 A So "most" I meant of the times I used 13 it, it was usually the DuraSeal product. It would 14 have been . . . 15 Q Okay. So let's -- let's take a -- take 16 a step back. 17 For craniotomies -- 18 A Uh-huh. 19 Q -- approximately how many craniotomies 20 have you done? 21 A Thousands. 22 Q And approximately what percentage after</p>	<p style="text-align: right;">Page 60</p> <p>1 So it's very dependent on what type of 2 cranial operation you're talking about. 3 Q Okay. To make sure we're clear, 4 approximately 100 percent of transsphenoidal 5 surgeries -- 6 A That's correct. 7 Q -- you've used a dural sealant in? 8 A That's right. 9 And there are other cranial operations 10 which involve the skull base or other anatomic 11 spaces where the use is nearly 100 percent. There 12 are other cranial operations that it's unusual; 13 i.e., less than 10 percent of the time you'd be -- 14 would I use a dural sealant product of any type. 15 Q And in -- including transsphenoidals 16 and craniotomies, in craniotomies approximately 17 what percent of the procedures you perform do you 18 use any type of dural sealant? 19 A I think that's -- I understand that to 20 be the same question, and I think I would estimate 21 around 10 percent of cases -- 22 Q Okay.</p>
<p style="text-align: right;">Page 59</p> <p>1 DuraSeal was available did you use DuraSeal on? 2 MR. ALTHERR: Object to the form. 3 THE WITNESS: I -- I -- I don't -- I 4 certainly don't know the exact number. 5 BY MR. HUGHES: 6 Q Approximate percentage. 7 A 10 percent. 8 Q Okay. So is it fair to say that -- 9 well, take a step back. 10 What percent of craniotomies that you 11 have conducted would -- did you use a dural 12 sealant on? 13 A And I'm just going to -- just to 14 clarify cranial surgeries, which I think we've 15 agreed is what you mean by craniotomies. And I'm 16 making that point because transsphenoidal 17 operations are certainly not an operation on the 18 cranial portion, but it's a cranial surgery at 19 that. And that percentage would be close to 20 100 percent. 21 Other cranial operations, the number 22 would be much, much lower.</p>	<p style="text-align: right;">Page 61</p> <p>1 A -- around 10 percent of cranial 2 surgeries a dural sealant product is used. 3 Q Do you ever use fiber and glue in that 4 10 percent of cases? 5 A I have used fiber and glue as a dural 6 sealant, yes. 7 Q Within that 10 percent of cases, 8 approximately how many have you used fiber and 9 glue in? 10 A At a time we used it in all 10 percent 11 or all fraction of dural sealant products because 12 it was all that was available. 13 Q What time was that? 14 A Prior to the release of DuraSeal or 15 prior to the integration of DuraSeal into the 16 practice I was in at the time. 17 Q Okay. So approximately when that was? 18 A Between 1998 and 2002. 19 Q Okay. 20 A And I would say -- I'm sorry. I would 21 say there was also some overlap, so it wasn't a 22 hard stop on the use of Floseal -- I beg your</p>

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1 pardon, with fiber and glue to transition
 2 100 percent to DuraSeal.
 3 **Q And the -- what was the product you**
 4 **just mentioned? Coseal?**
 5 A No.
 6 **Q Okay. And the fiber and glue that**
 7 **you've used in craniotomies, was that used**
 8 **off-label from the FDA label?**
 9 A I don't know the labeling. I believe
 10 it was off-label.
 11 **Q And when you've used DuraSeal -- I**
 12 **believe you previously testified you've used**
 13 **DuraSeal in spinal surgeries; is that correct?**
 14 A That's correct.
 15 **Q And do you know whether that was**
 16 **off-label?**
 17 A It is my understanding -- I don't know
 18 if that was off-label at the time. I'm not
 19 familiar with what the original labeling was for
 20 DuraSeal, did it include spinal applications. I
 21 don't know that for certain.
 22 **Q In the -- currently are you aware of**

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1 **what the labeling for DuraSeal is?**
 2 A My understanding is that DuraSeal is
 3 indicated for cranial operations and a dural
 4 sealant separable from spinal -- not spinal
 5 applications.
 6 **Q So in the time when DuraSeal was**
 7 **indicated for cranial operations separate from**
 8 **spinal operations, did you ever use it in spinal**
 9 **operations?**
 10 A Yes, I believe I did.
 11 **Q And that was an off-label use?**
 12 A I believe it was. Again, I think I've
 13 said I don't -- I do not know what the original --
 14 I'm not familiar with what the original DuraSeal
 15 FDA labeling was. It's possible that at the time
 16 it was released, for example, it was indicated for
 17 spinal operations. I'm just not aware of that.
 18 **Q But during the time frame when you know**
 19 **that the DuraSeal product has been indicated for**
 20 **not -- strike that.**
 21 **During the time frame that you know the**
 22 **DuraSeal product was not indicated for spinal use,**

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1 **you've used it for spinal use?**
 2 A I don't think I -- I would not agree
 3 with that statement. You used the word
 4 "indicated."
 5 **Q When I say "indicated," I mean on-label**
 6 **use, FDA approval.**
 7 A Okay. Would you repeat it?
 8 **Q Sure.**
 9 **So during the time frame that you know**
 10 **DuraSeal was not indicated for spinal use, you've**
 11 **used it for spinal use?**
 12 A My understanding is that there was a
 13 period of time when the FDA approval for DuraSeal
 14 may not have included spinal applications. And,
 15 yes, I believe it's very possible, if not likely,
 16 that we used it for spinal applications in an
 17 off-label use.
 18 **Q Okay. When was the last time you've**
 19 **used the DuraSeal product for a spinal surgery?**
 20 A In the last two weeks -- in the last
 21 ten days. I could, you know, get an exact day for
 22 you, but --

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1 **Q No.**
 2 A -- very recently.
 3 **Q That's okay.**
 4 **And that's -- just to make sure, we had**
 5 **a discussion with products a second ago. That was**
 6 **the regular DuraSeal product you've used in the**
 7 **last two weeks for a spinal indication?**
 8 A I don't recall which DuraSeal product
 9 it was.
 10 **Q A second ago we talked about DuraSeal**
 11 **versus Xact in using the terminology.**
 12 A Yes, sir.
 13 **Q So since we had that discussion, I've**
 14 **been using the word "DuraSeal" referring to the**
 15 **regular DuraSeal product.**
 16 A Yes, sir.
 17 **Q Do you have any clarifications or**
 18 **restatements in your testimony in that**
 19 **understanding?**
 20 A I do not.
 21 **Q So in -- when was the last time that**
 22 **you used the regular DuraSeal product for a spinal**

<p style="text-align: right;">Page 66</p> <p>1 surgery?</p> <p>2 A I believe it was in the last two weeks.</p> <p>3 Q Okay. And that would have been an</p> <p>4 off-label use?</p> <p>5 A If it was the regular DuraSeal, it</p> <p>6 would have been an off-label use. I just don't</p> <p>7 know for certain which DuraSeal product it was. I</p> <p>8 can't say with certainty was it DuraSeal, was it</p> <p>9 DuraSeal Xact.</p> <p>10 Q Why not?</p> <p>11 A I just don't have the patient's medical</p> <p>12 record in front of me.</p> <p>13 Q Are both available to you as a surgeon</p> <p>14 at your hospital?</p> <p>15 A I believe they are.</p> <p>16 Q When I say "both," I mean DuraSeal and</p> <p>17 DuraSeal Xact.</p> <p>18 A Understood. And I believe they are.</p> <p>19 Q When was the last time that you've</p> <p>20 used -- when was the last time that you know</p> <p>21 you've used the regular DuraSeal product in a</p> <p>22 spinal surgery?</p>	<p style="text-align: right;">Page 68</p> <p>1 "problem."</p> <p>2 BY MR. HUGHES:</p> <p>3 Q In your medical opinion --</p> <p>4 A Uh-huh.</p> <p>5 Q -- would you . . .</p> <p>6 (Sotto voce discussion.)</p> <p>7 BY MR. HUGHES:</p> <p>8 Q In your -- strike that.</p> <p>9 In your opinion, is DuraSeal and</p> <p>10 DuraSeal Xact interchangeable for medical</p> <p>11 procedures?</p> <p>12 A No.</p> <p>13 Q In your opinion, is DuraSeal and</p> <p>14 DuraSeal Xact interchangeable for spinal</p> <p>15 procedures?</p> <p>16 A They're not interchangeable.</p> <p>17 Q In your opinion --</p> <p>18 A For procedures, period. There's a</p> <p>19 difference between them -- the devices.</p> <p>20 Q In your opinion -- strike that.</p> <p>21 As a surgeon, would you have any</p> <p>22 apprehension of using the regular DuraSeal product</p>
<p style="text-align: right;">Page 67</p> <p>1 A I don't recall.</p> <p>2 Q Have you ever used the regular DuraSeal</p> <p>3 product in a spinal surgery?</p> <p>4 A I think that's a question we've --</p> <p>5 you've asked previously. And, yes, I believe that</p> <p>6 prior -- prior surgeries I used DuraSeal distinct</p> <p>7 from Xact in spinal operations.</p> <p>8 Q And in the last year, is it fair to say</p> <p>9 you've used DuraSeal distinct from Xact in a</p> <p>10 spinal surgery?</p> <p>11 A I don't think it's fair to say. I</p> <p>12 don't know that for certain at all.</p> <p>13 Q Why not?</p> <p>14 A Because it would require going back to</p> <p>15 every patients' medical records and, you know,</p> <p>16 accessing that to find out the answer to that</p> <p>17 question, and I haven't done that.</p> <p>18 Q In your medical opinion, do you believe</p> <p>19 there is a problem using the DuraSeal apart from</p> <p>20 the Xact product in a spinal surgery?</p> <p>21 MR. ALTHERR: Object to the form.</p> <p>22 THE WITNESS: You'd have to define</p>	<p style="text-align: right;">Page 69</p> <p>1 in a spinal surgery today?</p> <p>2 A If the Xact were available, yes.</p> <p>3 Q What if the Xact was not available?</p> <p>4 A Then better to use an off-label device</p> <p>5 as was done previously and I'm sure is routinely</p> <p>6 practiced. In a situation where you don't have</p> <p>7 both available, I believe it's preferable to use</p> <p>8 an off-label product than not use a dural sealant.</p> <p>9 Q So when DuraSeal Xact is not available</p> <p>10 to a surgeon, is the -- it can be appropriate for</p> <p>11 the surgeon to use the regular DuraSeal product in</p> <p>12 a spinal surgery?</p> <p>13 A Yes. I think off-label use of DuraSeal</p> <p>14 may be appropriate -- appropriate and reasonable</p> <p>15 in certain situations.</p> <p>16 Q And would a fiber and glue be</p> <p>17 appropriate to be used in a spinal surgery?</p> <p>18 MR. ALTHERR: Object to the form.</p> <p>19 THE WITNESS: Yeah, I could -- I could</p> <p>20 easily give you a scenario where it would be</p> <p>21 appropriate. And if you'd like, I can give you</p> <p>22 some examples.</p>

<p style="text-align: right;">Page 70</p> <p>1 BY MR. HUGHES:</p> <p>2 Q What is an example?</p> <p>3 A An example would be if you're</p> <p>4 practicing in an austere environment where you</p> <p>5 have no dural sealant and the only thing available</p> <p>6 to you was fiber and glue and you have a surgical</p> <p>7 procedure which requires -- or a dural sealant is</p> <p>8 indicated, it would be entirely reasonable to use</p> <p>9 that even knowing that elsewhere DuraSeal and</p> <p>10 other dural sealants would be available and FDA</p> <p>11 approved, et cetera.</p> <p>12 Q And going back to the discussion we</p> <p>13 were just having, there are two different</p> <p>14 products, DuraSeal regular and DuraSeal Xact;</p> <p>15 correct?</p> <p>16 A That's my understanding, yes.</p> <p>17 Q And you don't know when you use a</p> <p>18 DuraSeal product which one it is?</p> <p>19 A It's possible you don't know. You have</p> <p>20 to ask. You -- they're not identified. They</p> <p>21 don't have a label on the material that I'm aware</p> <p>22 of. So -- so, yes, it's possible to use it</p>	<p style="text-align: right;">Page 72</p> <p>1 know 100 percent what it is.</p> <p>2 Q And when you say relabeling, you mean</p> <p>3 it was relabeled in the surgical theater shortly</p> <p>4 before the procedure or during the procedure?</p> <p>5 A That's right. A local anesthetic is</p> <p>6 drawn up out of a bottle with a label. It's put</p> <p>7 in a tube and relabeled with a sticker that</p> <p>8 somebody writes on it to confirm that it is in</p> <p>9 that tube what it was off the field so that</p> <p>10 multiple things can be identified, so . . .</p> <p>11 Q Understood. Understood.</p> <p>12 Of the spinal surgeries that you</p> <p>13 perform, approximately what percent do you use a</p> <p>14 dural sealant in?</p> <p>15 A Again, that answer is very dependent on</p> <p>16 which spinal procedures. There's some spinal</p> <p>17 procedures that it's used in 100 percent. Any</p> <p>18 intradural procedure with rare exception --</p> <p>19 intradural spinal procedure, it's used.</p> <p>20 I've been in environments where we're</p> <p>21 routinely taking care of wounds that transgress</p> <p>22 the dural layer. It's used in nearly 100 percent</p>
<p style="text-align: right;">Page 71</p> <p>1 without knowing what you're using.</p> <p>2 Q When you said "they don't have a label</p> <p>3 on the material," what do you mean by that?</p> <p>4 A Well, the packaging might have a label,</p> <p>5 but it might be passed to you in the surgical</p> <p>6 field without a label visible to you.</p> <p>7 So it may seem hard to believe you</p> <p>8 don't know what you're using, but things are</p> <p>9 passed in the surgical field and relabeled by</p> <p>10 someone routinely. So someone off the field out</p> <p>11 of my view or out of the surgeon's view is</p> <p>12 routinely opening a product. And there's verbal</p> <p>13 confirmation of what you're asking for, and many</p> <p>14 times medications are relabeled, but that isn't --</p> <p>15 for example, if you implant a certain device, it</p> <p>16 may or may not have the actual size written on it.</p> <p>17 And a liquid isn't identified if it's in a tube,</p> <p>18 for example.</p> <p>19 So sometimes it's easily identifiable.</p> <p>20 Other times, as hard as it is to understand, that</p> <p>21 may be -- or hard to believe, it's possible to use</p> <p>22 something that you haven't clarified or you don't</p>	<p style="text-align: right;">Page 73</p> <p>1 of the time. If you ask in my entire career</p> <p>2 lumping all spinal procedures together, I think a</p> <p>3 reasonable estimate would again be in the area of</p> <p>4 10 percent.</p> <p>5 This is very dependent on what</p> <p>6 someone's practice is. There are surgeons who</p> <p>7 exclusively or nearly exclusively practice</p> <p>8 intradural surgeries on tumors, for example. And</p> <p>9 their use -- they might can -- they might</p> <p>10 respond that they nearly use it 100 percent of the</p> <p>11 time.</p> <p>12 There are other orthopedic spine</p> <p>13 surgeons, for example, that it's much more rare</p> <p>14 for them to use a dural sealant because, in</p> <p>15 general, they don't do intradural spinal</p> <p>16 surgeries -- in general. And their answer might</p> <p>17 be on the order of less than 1 percent.</p> <p>18 Q And when you're saying they might use a</p> <p>19 dural sealant --</p> <p>20 A Yes.</p> <p>21 Q -- what is the universe of possible</p> <p>22 dural sealants they would use?</p>

<p style="text-align: right;">Page 74</p> <p>1 A I can't speculate on what their -- the</p> <p>2 universe of dural sealants someone else might use.</p> <p>3 Q So you can't -- so you have no opinion</p> <p>4 on the universe of dural sealants that a surgeon</p> <p>5 might use in a spinal procedure?</p> <p>6 A In my practice currently, as we've</p> <p>7 discussed, it's possible to use the HyperBranch</p> <p>8 product. It's possible to use the Integra</p> <p>9 DuraSeal, DuraSeal Xact or -- or Tisseel, a fiber</p> <p>10 and glue --</p> <p>11 Q And Tisseel --</p> <p>12 A -- more generically.</p> <p>13 Q Tisseel is a type of fiber and glue?</p> <p>14 A I believe it's a brand name for it, so</p> <p>15 fiber and glue is probably more accurate.</p> <p>16 Q Okay.</p> <p>17 A I don't know that it would always be</p> <p>18 Tisseel that's available to somebody.</p> <p>19 Fiber and glue is probably the term I</p> <p>20 should use to be more accurate.</p> <p>21 Q But you have no opinion -- actually,</p> <p>22 strike that.</p>	<p style="text-align: right;">Page 76</p> <p>1 can't speak to that. I'm not commenting to that.</p> <p>2 Do I know it's available in the European market?</p> <p>3 No, I'm not.</p> <p>4 I can say in general what my practice</p> <p>5 has been currently, what it was in the last 15</p> <p>6 years, and what I understand to be available to</p> <p>7 surgeons in the United States and North America</p> <p>8 currently.</p> <p>9 BY MR. HUGHES:</p> <p>10 Q So looking at the United States, what</p> <p>11 is the universe of dural sealants that a spinal</p> <p>12 surgeon would have available to them?</p> <p>13 A I would repeat the same answer. The</p> <p>14 three I -- dural sealants I mentioned fiber, so</p> <p>15 fiber and glue, the HyperBranch product, and the</p> <p>16 Integra which includes DuraSeal and DuraSeal Xact.</p> <p>17 Q And do you have an opinion on</p> <p>18 approximately how many times spinal surgeons in</p> <p>19 the United States use any of those given products?</p> <p>20 A I think I answered that in -- it's very</p> <p>21 dependent on what their practice is.</p> <p>22 Q But sitting here today, do you have an</p>
<p style="text-align: right;">Page 75</p> <p>1 You don't know generally in the field</p> <p>2 of surgeons what -- the universe of possible dural</p> <p>3 sealants that a surgeon would use in a spinal</p> <p>4 procedure?</p> <p>5 MR. ALTHERR: Object to form.</p> <p>6 THE WITNESS: Would you repeat that</p> <p>7 question?</p> <p>8 BY MR. HUGHES:</p> <p>9 Q Yeah. Strike that.</p> <p>10 You don't know the universe of possible</p> <p>11 dural sealants that a surgeon would use in a</p> <p>12 spinal indication?</p> <p>13 Strike that, the "indication" word.</p> <p>14 You don't know the universe of dural</p> <p>15 sealants that a surgeon would use in a spinal</p> <p>16 surgery?</p> <p>17 MR. ALTHERR: Object to the form.</p> <p>18 THE WITNESS: Yeah, I'm not sure I</p> <p>19 understand the question. I've stated what I have</p> <p>20 currently available. I think that spinal</p> <p>21 surgeons -- and, again, do I know what's available</p> <p>22 to spinal surgeons in South America? I -- I -- I</p>	<p style="text-align: right;">Page 77</p> <p>1 opinion on the number of possible surgeon --</p> <p>2 possible -- strike that.</p> <p>3 Sitting here today, do you have an</p> <p>4 opinion on the number of times a surgeon in the</p> <p>5 United States -- surgeons, generally, in the</p> <p>6 United States use any of those four products you</p> <p>7 just mentioned?</p> <p>8 MR. ALTHERR: Object to the form.</p> <p>9 THE WITNESS: My estimate would be</p> <p>10 somewhere in the single digit percentages of all</p> <p>11 spinal surgeries performed in the United States so</p> <p>12 I guess between 1 and 9 percent, somewhere in an</p> <p>13 estimate.</p> <p>14 I said there are some surgeons that use</p> <p>15 it less than 1 percent of the time or 1 percent of</p> <p>16 the time. There are other people whose practices</p> <p>17 are different that use it probably pretty</p> <p>18 frequently.</p> <p>19 BY MR. HUGHES:</p> <p>20 Q And what is the basis of that opinion?</p> <p>21 A My knowledge of the neurosurgical</p> <p>22 practice and the spinal surgery practice, the</p>

<p>1 national history of spinal diseases.</p> <p>2 Q So looking at cranial surgeries --</p> <p>3 A Uh-huh.</p> <p>4 Q -- what is -- what is the universe of</p> <p>5 dural sealants available for cranial surgeries?</p> <p>6 A Same answer. I can -- I'll repeat it</p> <p>7 if you want. Fiber and glue, the HyperBranch</p> <p>8 product, the DuraSeal. And I think there are some</p> <p>9 people that -- it's possible that not every</p> <p>10 surgeon has access to both DuraSeal and DuraSeal</p> <p>11 Xact. It's possible that -- it's likely that not</p> <p>12 every hospital has access to all three products --</p> <p>13 Q Okay.</p> <p>14 A -- so . . .</p> <p>15 MR. HUGHES: We've been going for a</p> <p>16 little bit over an hour now. It might be a good</p> <p>17 time for a break.</p> <p>18 THE WITNESS: Sounds great.</p> <p>19 THE VIDEOGRAPHER: The time is</p> <p>20 10:07:41 a.m. We are now off the record.</p> <p>21 (Recess -- 10:07 a.m.)</p> <p>22 (After recess -- 10:19 a.m.)</p>	<p>Page 78</p> <p>Page 80</p> <p>1 A I think you also asked that, and I</p> <p>2 don't have the medical record in front of me.</p> <p>3 Q And when you get ready for a surgery,</p> <p>4 do you request in advance a certain product?</p> <p>5 A Very common to request certain products</p> <p>6 prior to surgery, yes.</p> <p>7 Q And when you're getting ready for a</p> <p>8 spinal surgery, do you request a specific DuraSeal</p> <p>9 or DuraSeal Xact?</p> <p>10 A Often do, yes.</p> <p>11 Q So you often will request to have</p> <p>12 DuraSeal or DuraSeal Xact specifically before you</p> <p>13 have a -- before performing a spinal surgery?</p> <p>14 A Excuse me. If -- if a surgery where</p> <p>15 you knew you were going to have an intradural</p> <p>16 portion of the surgery, usually someone will</p> <p>17 request the presence of DuraSeal because it may</p> <p>18 not be in the room. And for efficiency purposes,</p> <p>19 yes.</p> <p>20 Q So before someone is going to have a</p> <p>21 spinal surgery, they would request the presence of</p> <p>22 DuraSeal regular to be in the room?</p>
<p>Page 79</p> <p>1 (Mr. Pivovar not present.)</p> <p>2 THE VIDEOGRAPHER: The time is</p> <p>3 approximately 10:19:38 a.m. We are now on the</p> <p>4 record.</p> <p>5 BY MR. HUGHES:</p> <p>6 Q Dr. Rivet, before we broke, we were</p> <p>7 discussing your use of the DuraSeal and DuraSeal</p> <p>8 Xact product.</p> <p>9 Do you remember that discussion?</p> <p>10 A I think so, yes.</p> <p>11 Q And you testified that in the last week</p> <p>12 you have used the DuraSeal product or DuraSeal</p> <p>13 Xact product in a spinal surgery; is that</p> <p>14 accurate?</p> <p>15 A I think I said -- I estimated ten to 14</p> <p>16 days, but I said recently, yes.</p> <p>17 Q And do you know which of the two</p> <p>18 products you used?</p> <p>19 A I think you asked that, and the answer</p> <p>20 is I'm not certain which product I used.</p> <p>21 Q And why are you not certain which</p> <p>22 product you used?</p>	<p>Page 81</p> <p>1 A I don't think you added in intradural</p> <p>2 procedure.</p> <p>3 So if -- if a surgery that you know</p> <p>4 you're going to have a transdural portion, the</p> <p>5 dura will be opened, it would be routine for a</p> <p>6 surgeon to request a dural sealant product be</p> <p>7 available for the surgery, yes.</p> <p>8 Q The last time you used the DuraSeal</p> <p>9 product, did you know that you were going to have</p> <p>10 an intradural procedure?</p> <p>11 A Yes.</p> <p>12 Q And did you request a dural sealant in</p> <p>13 advance?</p> <p>14 A I don't recall if I did or not.</p> <p>15 Q But you just testified that a surgeon</p> <p>16 would request in advance to have a dural sealant</p> <p>17 available?</p> <p>18 A Yes, typically people do request a</p> <p>19 dural sealant. I believe typically surgeons</p> <p>20 request the devices they'll need during surgery,</p> <p>21 and in a procedure where one knows you're going to</p> <p>22 have a transdural portion, yes, the typical</p>

<p style="text-align: right;">Page 82</p> <p>1 practice would be to make the staff aware of that</p> <p>2 so it was available.</p> <p>3 Q So in your practice, when you know</p> <p>4 you're going to have a transdural -- pardon me, an</p> <p>5 intradural procedure, do you request to have a</p> <p>6 dural sealant available?</p> <p>7 A Yes, sir, I try to.</p> <p>8 Q And do you specifically request</p> <p>9 DuraSeal regular or DuraSeal Xact for a spinal</p> <p>10 surgery?</p> <p>11 A If I knew it was going to be a spinal</p> <p>12 surgery and I had Xact available, that's what I</p> <p>13 would request, yes.</p> <p>14 Q But you just said when you performed</p> <p>15 your last surgery, you were not aware if it was</p> <p>16 DuraSeal or DuraSeal Xact; is that accurate?</p> <p>17 A That's correct.</p> <p>18 Q So you didn't know which product you</p> <p>19 were using?</p> <p>20 A Again, I think you've asked that</p> <p>21 question; this is the third time.</p> <p>22 On the most recent case where I used</p>	<p style="text-align: right;">Page 84</p> <p>1 MR. ALTHERR: -- form.</p> <p>2 BY MR. HUGHES:</p> <p>3 Q -- DuraSeal product, that is?</p> <p>4 MR. ALTHERR: Object -- object to the</p> <p>5 form.</p> <p>6 THE WITNESS: Yes.</p> <p>7 BY MR. HUGHES:</p> <p>8 Q And yet you just testified you didn't</p> <p>9 know which product, DuraSeal or DuraSeal Xact, you</p> <p>10 were using when you used it in a spinal surgery?</p> <p>11 A That's correct.</p> <p>12 Q Do you always know if you're using</p> <p>13 DuraSeal or DuraSeal Xact in a spinal surgery?</p> <p>14 A I think as evidenced by my last answer,</p> <p>15 no.</p> <p>16 Q So you do not always know if you're</p> <p>17 using DuraSeal or DuraSeal Xact when you perform a</p> <p>18 spinal surgery?</p> <p>19 A Correct.</p> <p>20 Q Earlier you said that there are two</p> <p>21 different devices, and you referred to DuraSeal</p> <p>22 and DuraSeal Xact as two different devices.</p>
<p style="text-align: right;">Page 83</p> <p>1 it, I'm not aware of which product I used. I</p> <p>2 don't have the medical record in front of me.</p> <p>3 Q And are you aware that there are</p> <p>4 different swelling effects of the DuraSeal regular</p> <p>5 versus Xact product?</p> <p>6 A Yes.</p> <p>7 Q And are you aware that there can be</p> <p>8 negative ramifications of using the DuraSeal</p> <p>9 product in a spinal surgery?</p> <p>10 MR. ALTHERR: Object to the form.</p> <p>11 THE WITNESS: Would you repeat the</p> <p>12 question?</p> <p>13 BY MR. HUGHES:</p> <p>14 Q Are you aware that there can be</p> <p>15 negative ramifications of using the DuraSeal</p> <p>16 product in a spinal surgery --</p> <p>17 MR. ALTHERR: Object to --</p> <p>18 BY MR. HUGHES:</p> <p>19 Q -- the --</p> <p>20 MR. ALTHERR: -- the --</p> <p>21 BY MR. HUGHES:</p> <p>22 Q -- regular --</p>	<p style="text-align: right;">Page 85</p> <p>1 Do you remember that?</p> <p>2 A Yes, I do think I remember I used that</p> <p>3 word.</p> <p>4 Q What did you mean by the word "device"?</p> <p>5 A As distinct from an instrument that</p> <p>6 won't be placed in a patient and distinct from</p> <p>7 tissue. Something you're using during a</p> <p>8 procedure.</p> <p>9 Q And is there a difference between the</p> <p>10 DuraSeal regular and DuraSeal Xact?</p> <p>11 A Yes, my understanding there is a</p> <p>12 difference in the formulation between the two.</p> <p>13 Q The formulation of the hydrogel?</p> <p>14 A Correct.</p> <p>15 Q And is there a difference in the</p> <p>16 applicator between DuraSeal and DuraSeal Xact?</p> <p>17 A I don't -- there may be.</p> <p>18 Q And what -- what is that difference?</p> <p>19 A I don't know. I'm saying there may be</p> <p>20 a difference.</p> <p>21 Q Okay. And are you familiar with the</p> <p>22 MicroMist device?</p>

<p style="text-align: right;">Page 86</p> <p>1 A Yes.</p> <p>2 Q What is the MicroMist device?</p> <p>3 A It's a device that's used to help</p> <p>4 aerosolize or apply the DuraSeal.</p> <p>5 Q Do you use the MicroMist device?</p> <p>6 A I have, yes.</p> <p>7 Q Do you use it with DuraSeal regular?</p> <p>8 A Yes.</p> <p>9 Q Do you use it with DuraSeal Xact?</p> <p>10 A I don't know that I've ever used it</p> <p>11 with DuraSeal Xact. So it's --</p> <p>12 Q Do you --</p> <p>13 A -- poss- --</p> <p>14 Q -- use --</p> <p>15 A -- -ible, but I don't recall it.</p> <p>16 Q Do you use the MicroMist device with</p> <p>17 DuraSeal regular in a spinal surgery?</p> <p>18 A I don't recall using the MicroMist</p> <p>19 device with DuraSeal regular during a spinal</p> <p>20 surgery.</p> <p>21 Q Do you recall using the -- so -- strike</p> <p>22 that.</p>	<p style="text-align: right;">Page 88</p> <p>1 A No.</p> <p>2 Q In the last year?</p> <p>3 A I don't believe so.</p> <p>4 Q In the last five years?</p> <p>5 A Yes.</p> <p>6 Q In the last three years?</p> <p>7 A Yes, likely.</p> <p>8 Q Approximately -- of the percentage of</p> <p>9 DuraSeal regular surgeries you use in a spinal --</p> <p>10 for a craniotomy -- strike that.</p> <p>11 Approximately -- of the -- strike that</p> <p>12 again.</p> <p>13 Of the regular DuraSeal product you use</p> <p>14 in craniotomies, approximately how many -- what</p> <p>15 percent of those do you use the MicroMist device</p> <p>16 with?</p> <p>17 A Approximately 5 to 10 percent.</p> <p>18 Q Is it fair to say you're not aware of</p> <p>19 any difference between the applicator of the</p> <p>20 DuraSeal regular and DuraSeal Xact product?</p> <p>21 A I believe that's what I answered. I</p> <p>22 don't -- there may be a difference. I'm not aware</p>
<p style="text-align: right;">Page 87</p> <p>1 So you never used the DuraSeal regular</p> <p>2 with MicroMist in a spinal surgery?</p> <p>3 MR. ALTHERR: Object to the form.</p> <p>4 THE WITNESS: Yeah, I think it's</p> <p>5 impossible for me to answer that. We're talking</p> <p>6 about thousands of cases, hundreds of cases and</p> <p>7 over a period of years.</p> <p>8 So it is certainly possible. Do I</p> <p>9 recall a case? No, I do not.</p> <p>10 BY MR. HUGHES:</p> <p>11 Q Okay. And you -- is it accurate you do</p> <p>12 not recall using the MicroMist device with a</p> <p>13 DuraSeal Xact product?</p> <p>14 A That's correct. I do not recall.</p> <p>15 Q Do you recall using the MicroMist</p> <p>16 device with DuraSeal regular in a craniotomy?</p> <p>17 A Yes.</p> <p>18 Q When is the last time you used the</p> <p>19 MicroMist device in a craniotomy with DuraSeal</p> <p>20 regular?</p> <p>21 A I don't re- -- I don't recall.</p> <p>22 Q In the last week?</p>	<p style="text-align: right;">Page 89</p> <p>1 of what that difference is.</p> <p>2 Q But you -- is it accurate to say you</p> <p>3 just testified there's a difference in the</p> <p>4 hydrogel between DuraSeal regular and DuraSeal</p> <p>5 Xact?</p> <p>6 A Yes.</p> <p>7 Q Okay. What is your current title and</p> <p>8 role right now?</p> <p>9 A My title is associate professor in the</p> <p>10 Department of Neurosurgery of Virginia</p> <p>11 Commonwealth University.</p> <p>12 Q And what are your duties in that role?</p> <p>13 A My duties are performing clinical</p> <p>14 neurosurgery, research, and a variety of teaching</p> <p>15 roles to include medical students, graduate</p> <p>16 students, and the neurosurgical residents as well</p> <p>17 as residents from other departments.</p> <p>18 Q And are you currently an assistant</p> <p>19 professor at the United Services University,</p> <p>20 University of Health Sciences in Bethesda,</p> <p>21 Maryland?</p> <p>22 A Yes, I am.</p>

<p style="text-align: right;">Page 90</p> <p>1 Q And what are your roles and duties in</p> <p>2 that position?</p> <p>3 A They overlap with my roles at Virginia</p> <p>4 Commonwealth University. The things that are</p> <p>5 specific to that employment are doing -- be</p> <p>6 involved in teaching in -- medical students and</p> <p>7 residents from the military, the Armed Services.</p> <p>8 Q And are those residents -- do you</p> <p>9 interact with them in Richmond, or do you interact</p> <p>10 with them in Bethesda?</p> <p>11 A I interact with those residents in</p> <p>12 Richmond and typically in Portsmouth, Virginia.</p> <p>13 (Deposition Exhibit 411 was marked for</p> <p>14 identification and attached to the transcript.)</p> <p>15 BY MR. HUGHES:</p> <p>16 Q Dr. Rivet, the court reporter just</p> <p>17 handed you what's been marked as Exhibit 4-1-1,</p> <p>18 411.</p> <p>19 Do you recognize this document?</p> <p>20 A I do.</p> <p>21 I'm sorry to interrupt. Would it be</p> <p>22 possible to get my reading glasses? I apologize.</p>	<p style="text-align: right;">Page 92</p> <p>1 A Yes, sir.</p> <p>2 Q -- there's a date and a signature</p> <p>3 there. What is the date?</p> <p>4 A The date is August 24th, 2017.</p> <p>5 Q And is that your signature?</p> <p>6 A Yes, sir, it is.</p> <p>7 Q And as of August 24th, 2017, does this</p> <p>8 report contain a complete statement of all</p> <p>9 opinions expressed in this report and the basis</p> <p>10 and reasons for them?</p> <p>11 A Can you repeat the question?</p> <p>12 Q As of October 24, 2017, does this</p> <p>13 exhibit contain a complete statement of all</p> <p>14 opinions expressed in the report and the basis and</p> <p>15 reasons for them?</p> <p>16 A Would you say the date you said in the</p> <p>17 first sentence? "As of October" --</p> <p>18 Q 24th, 2017, which I believe is the date</p> <p>19 you signed the report.</p> <p>20 MR. ALTHERR: You said October.</p> <p>21 MR. HUGHES: I'm sorry. August.</p> <p>22 Strike that.</p>
<p style="text-align: right;">Page 91</p> <p>1 They're in my briefcase.</p> <p>2 MR. HUGHES: Can we go off the record,</p> <p>3 please?</p> <p>4 THE VIDEOGRAPHER: The time is</p> <p>5 10:29:58 a.m. We're --</p> <p>6 THE WITNESS: I'm --</p> <p>7 THE VIDEOGRAPHER: -- going --</p> <p>8 THE WITNESS: -- sorry.</p> <p>9 THE VIDEOGRAPHER: -- off the record.</p> <p>10 (Recess -- 10:29 a.m.)</p> <p>11 (After recess -- 10:31 a.m.)</p> <p>12 THE VIDEOGRAPHER: The time is</p> <p>13 10:31:54 a.m. We are now on the record.</p> <p>14 BY MR. HUGHES:</p> <p>15 Q Dr. Rivet, the court reporter has just</p> <p>16 handed you what's been marked as Exhibit 4-1-1,</p> <p>17 411.</p> <p>18 Do you recognize this document?</p> <p>19 A I do.</p> <p>20 Q What is this document?</p> <p>21 A This is my expert report.</p> <p>22 Q If you turn to page 23 of the report --</p>	<p style="text-align: right;">Page 93</p> <p>1 BY MR. HUGHES:</p> <p>2 Q As of August 24th, 2017, does this</p> <p>3 exhibit contain a complete statement of all</p> <p>4 opinions expressed in this report and the bases</p> <p>5 and reasons for them?</p> <p>6 A I believe it does.</p> <p>7 Q And as of August 24th, 2017, does this</p> <p>8 exhibit contain all the facts or data considered</p> <p>9 in forming your opinions?</p> <p>10 A I believe it summarizes what I used to</p> <p>11 reach my opinions, yes.</p> <p>12 Q But does it contain all the facts or</p> <p>13 data considered in forming your opinions?</p> <p>14 MR. ALTHERR: Object to the form.</p> <p>15 THE WITNESS: No.</p> <p>16 BY MR. HUGHES:</p> <p>17 Q It does not contain --</p> <p>18 A That's correct.</p> <p>19 Q -- all the facts or data considered in</p> <p>20 forming your opinions?</p> <p>21 A That's correct.</p> <p>22 Q This Exhibit 411, your expert report of</p>

<p style="text-align: right;">Page 94</p> <p>1 Dennis J. Rivet that you signed on August 24th,</p> <p>2 2017, does not contain all the facts or data</p> <p>3 considered in forming your opinions?</p> <p>4 A By that -- correct. What I mean is</p> <p>5 there -- for example, in -- I'll give you an exact</p> <p>6 paragraph. Maybe I'm being too specific.</p> <p>7 Paragraph 35 I say, Furthermore, I have</p> <p>8 spoken with my colleagues at VCU who use the</p> <p>9 Adherus AutoSpray Extended Tip.</p> <p>10 The context of those exact discussions,</p> <p>11 et cetera, they are -- that's the only summary of</p> <p>12 those discussions, for example.</p> <p>13 So if by referencing that, that is</p> <p>14 sufficient that that's -- what formed my opinion</p> <p>15 is multiple conversations, that's -- that's what I</p> <p>16 mean.</p> <p>17 Q Is that the only location where you</p> <p>18 have not given all of the facts or data considered</p> <p>19 in forming your opinions in this report?</p> <p>20 A Yes, that's the only thing I'm aware</p> <p>21 of.</p> <p>22 Q Are there any errors or typos in this</p>	<p style="text-align: right;">Page 96</p> <p>1 Extended Tip (ET) Dural Sealant?</p> <p>2 That's the only information that was</p> <p>3 contained in this report?</p> <p>4 A Correct. I think you just read</p> <p>5 paragraph 35, yes.</p> <p>6 Q So why did you withhold information</p> <p>7 from this report?</p> <p>8 MR. ALTHERR: Object to the form.</p> <p>9 THE WITNESS: Yeah, I didn't withhold</p> <p>10 any information.</p> <p>11 BY MR. HUGHES:</p> <p>12 Q Why did you not include the substance</p> <p>13 of these discussions of colleagues at VCU in this</p> <p>14 report?</p> <p>15 A Just summarizing that I had the</p> <p>16 conversations, I think is sufficient.</p> <p>17 Q Summarizing you had the conversations</p> <p>18 but not specifically stating any more detail with</p> <p>19 those conversations?</p> <p>20 A Correct.</p> <p>21 Q So you didn't state who you spoke with;</p> <p>22 correct?</p>
<p style="text-align: right;">Page 95</p> <p>1 report other than the reference you just made to</p> <p>2 speaking with physicians at -- colleagues at VCU?</p> <p>3 A I don't -- I haven't seen any in my</p> <p>4 examination thus far.</p> <p>5 Q So you just said that this report does</p> <p>6 not contain all the facts or data used in forming</p> <p>7 your opinions in that it does not contain all of</p> <p>8 the information regarding your colleagues at VCU</p> <p>9 who you spoke with?</p> <p>10 MR. ALTHERR: Object to form.</p> <p>11 THE WITNESS: Correct. The substance</p> <p>12 of -- I simply summarized that I had conversations</p> <p>13 and the -- the -- and that's -- all it is is a</p> <p>14 summary.</p> <p>15 BY MR. HUGHES:</p> <p>16 Q So you just -- the only thing you</p> <p>17 provided in your report was a summary of the</p> <p>18 discussions you had with colleagues at VCU who</p> <p>19 used the AutoSpray -- pardon me. Strike that.</p> <p>20 So all you included in this report is a</p> <p>21 summary that stated I have spoken with -- to my</p> <p>22 colleagues at VCU who used the Adherus AutoSpray</p>	<p style="text-align: right;">Page 97</p> <p>1 A I don't believe I did.</p> <p>2 Q And you didn't state the substance of</p> <p>3 those conversations; correct?</p> <p>4 A That's right.</p> <p>5 Q And you didn't state how many</p> <p>6 conversations you had; correct?</p> <p>7 A That's right.</p> <p>8 And those are all great examples of the</p> <p>9 details that --</p> <p>10 Q And why did you not include that in</p> <p>11 this report?</p> <p>12 A Simply for purposes of brevity.</p> <p>13 Q You were concerned with having a report</p> <p>14 that would be too long if you contained those --</p> <p>15 the substance of those conversations?</p> <p>16 A No, I think summarizing it as we have</p> <p>17 is sufficient to relate that that's one of the</p> <p>18 things that allowed me to form the opinions.</p> <p>19 Q Summarizing that you had conversations</p> <p>20 allowed you to form the opinions stated in this</p> <p>21 report?</p> <p>22 A Summarizing that I had the</p>

<p style="text-align: right;">Page 98</p> <p>1 conversations is sufficient to disclose the things</p> <p>2 that I used to form my opinions.</p> <p>3 Q And what is the basis for your belief</p> <p>4 that that is sufficient?</p> <p>5 A My professional opinion.</p> <p>6 Q In your professional opinion as a</p> <p>7 surgeon?</p> <p>8 A As an expert witness.</p> <p>9 Q Your professional opinion as an expert</p> <p>10 witness. So you're a professional expert witness?</p> <p>11 A No.</p> <p>12 Q Are you a surgeon professionally?</p> <p>13 A Yes.</p> <p>14 Q So your professional opinion as an</p> <p>15 expert witness is it was sufficient to summarize</p> <p>16 the discussions with your colleagues at VCU rather</p> <p>17 than including any detail from those</p> <p>18 conversations?</p> <p>19 A That's right. I judge that to be a</p> <p>20 sufficient summary.</p> <p>21 Q And what is your basis for that</p> <p>22 sufficient summary -- strike --</p>	<p style="text-align: right;">Page 100</p> <p>1 Extended Tip (ET) Dural Sealant without giving the</p> <p>2 details of those discussions so HyperBranch may</p> <p>3 appropriately respond to those?</p> <p>4 MR. ALTHERR: Object to the form.</p> <p>5 THE WITNESS: Correct. It's my</p> <p>6 understanding that they'll be able to respond to</p> <p>7 any of my opinions.</p> <p>8 BY MR. HUGHES:</p> <p>9 Q It's your understanding that</p> <p>10 HyperBranch will be able to respond to any of your</p> <p>11 opinions?</p> <p>12 A To this report and my opinions,</p> <p>13 correct.</p> <p>14 Q But if all you stated was I have spoken</p> <p>15 to my colleagues at VCU who use the Adherus</p> <p>16 AutoSpray Extended Tip (ET) Dural Sealant, that</p> <p>17 was sufficient to allow HyperBranch to respond to</p> <p>18 the opinion?</p> <p>19 A To my opinion, yes.</p> <p>20 Q To the opinion that you spoke to your</p> <p>21 colleagues.</p> <p>22 A Correct.</p>
<p style="text-align: right;">Page 99</p> <p>1 MR. ALTHERR: Objection.</p> <p>2 BY MR. HUGHES:</p> <p>3 Q -- that.</p> <p>4 What is the basis of your belief that</p> <p>5 was sufficient -- a sufficient summary?</p> <p>6 MR. ALTHERR: Object to the form.</p> <p>7 THE WITNESS: It's my opinion.</p> <p>8 BY MR. HUGHES:</p> <p>9 Q And your opinion based on what?</p> <p>10 A A desire to convey the rationale for my</p> <p>11 opinions in the report judging this to be</p> <p>12 sufficient.</p> <p>13 Q And it was sufficient that you state</p> <p>14 that without giving HyperBranch an opportunity to</p> <p>15 respond to those opinions?</p> <p>16 MR. ALTHERR: Object to the form.</p> <p>17 THE WITNESS: I -- I don't know if</p> <p>18 that's sufficient.</p> <p>19 BY MR. HUGHES:</p> <p>20 Q So you don't know if it's sufficient to</p> <p>21 state a summary that you spoke with your</p> <p>22 colleagues at VCU regarding the Adherus AutoSpray</p>	<p style="text-align: right;">Page 101</p> <p>1 Q About a single product, the Adherus</p> <p>2 AutoSpray Extended Tip (ET) Dural Sealant;</p> <p>3 correct?</p> <p>4 A Correct. I'm sorry. You -- you --</p> <p>5 just -- I think a sentence ago you said to the</p> <p>6 opinion that I spoke to my colleagues. That --</p> <p>7 that is a fact that I spoke to my colleagues that</p> <p>8 allowed me to form my opinions.</p> <p>9 Q Oh.</p> <p>10 A I'm not sure -- I'm not trying to pick</p> <p>11 on the wording, but --</p> <p>12 Q But to respond to your opinions,</p> <p>13 doesn't HyperBranch need to know the facts or data</p> <p>14 considered in forming your opinions?</p> <p>15 A I don't know what they need, and I</p> <p>16 believe they have the basis of my opinions in this</p> <p>17 report.</p> <p>18 Q And the basis of your opinions in this</p> <p>19 report is that you spoke to your colleagues at VCU</p> <p>20 who used Adherus AutoSpray Extended Tip (ET) Dural</p> <p>21 Sealant?</p> <p>22 A Among other things, yes.</p>

<p style="text-align: right;">Page 102</p> <p>1 Q Regarding your discussions with your 2 colleagues at VCU who used the Adherus AutoSpray 3 Extended Tip (ET) Dural Sealant, is that sentence 4 the full extent of the facts or data contained in 5 your report regarding those conversations? 6 A Would you repeat that? 7 Q The sentence we have here in your 8 report at paragraph 35, I have spoken to my 9 colleagues at VCU who used the Adherus AutoSpray 10 Extended Tip (ET) Dural Sealant, is that statement 11 the full extent of the facts or data considered in 12 your report regarding those discussions? 13 MR. ALTHERR: Object to the form. 14 THE WITNESS: Yes. 15 BY MR. HUGHES: 16 Q Did you consult with anyone before you 17 chose to not contain the -- strike that. 18 Did you consult with anyone when you 19 chose to not contain any more information on the 20 discussions with colleagues at VCU in your report? 21 MR. ALTHERR: Object to the form. 22 THE WITNESS: No.</p>	<p style="text-align: right;">Page 104</p> <p>1 A Dr. Vega, V-E-G-A. 2 Q Anyone else? 3 A Dr. Brzezicki, B-R-Z-E-Z-I-C-K-I. 4 Q Anyone else? 5 A Ms. Pleasants, P-L-E-A-S-A-N-T-S, 6 Pleasants. 7 Q Anyone else? 8 A And I believe Dr. Broaddus, 9 B-R-O-A-D-D-U-S. 10 Q So this sentence in paragraph 35 we're 11 discussing, the colleagues at VCU who discussed 12 the -- their use of the Adherus AutoSpray Extended 13 Tip (ET) Dural Sealant with, that group consists 14 of Dr. Holloway, Dr. Vega, Dr. Brzezicki, 15 Ms. Pleasants and Dr. Broaddus? 16 A Correct. I should also add, I think, 17 depending on how you define VCU, there's a -- 18 there was a sales rep or distributor at VCU who I 19 don't know his name off the top of my head that I 20 spoke to about the possibility of using it. 21 Q And in this sentence in paragraph 35, 22 were you intending to reference the discussion</p>
<p style="text-align: right;">Page 103</p> <p>1 BY MR. HUGHES: 2 Q And that was your independent opinion 3 as an expert witness that you did not need to 4 provide any more information on these discussions 5 with colleagues at VCU? 6 MR. ALTHERR: Object to the form. 7 THE WITNESS: That's correct. 8 BY MR. HUGHES: 9 Q So let's talk about these discussions 10 with your colleagues at VCU. 11 Who did you talk to at VCU regarding -- 12 strike that. 13 The sentence in the paragraph 35, I 14 have spoken to my colleagues at VCU who used the 15 Adherus AutoSpray Extended Tip (ET) Dural Sealant, 16 which colleagues at VCU are you referring to in 17 this sentence? 18 A The residents and faculty in my 19 department. 20 Q Specifically who are those people? 21 A Dr. Holloway. 22 Q Anyone else?</p>	<p style="text-align: right;">Page 105</p> <p>1 with this sales rep? 2 MR. ALTHERR: Object to the form. 3 THE WITNESS: Potentially, yes. 4 BY MR. HUGHES: 5 Q Po- -- 6 A Yes. 7 Q -- -tentially? 8 A Yes. I'll say yes. 9 Q And you do not -- is Steve Rockwell, 10 that sales rep? 11 A I believe that's correct. 12 Q Is there anyone else that you were 13 attempting to identify in this sentence in 14 paragraph 35 that you spoke with regarding the 15 Adherus AutoSpray Extended Tip (ET) Dural Sealant? 16 A No, not that I can recall. 17 Q Is there anyone else who you spoke with 18 regarding the use of the Adherus AutoSpray 19 Extended Tip (ET) Dural Sealant that you relied 20 upon in forming your opinions in this report? 21 A No. 22 Q So the only people who you spoke with</p>

<p style="text-align: right;">Page 106</p> <p>1 regarding their use of the Adherus AutoSpray</p> <p>2 Extended Tip (ET) Dural Sealant in preparation for</p> <p>3 your report are Dr. Holloway; Dr. Veg- --</p> <p>4 Dr. Vega; Dr. Brzezicki; Ms. Pleasants;</p> <p>5 Dr. Broadus; and a sales rep, Steve Rockwell?</p> <p>6 A I believe that's correct, yes.</p> <p>7 Q And this sentence refers to the Adherus</p> <p>8 AutoSpray Extended Tip (ET) Dural Sealant.</p> <p>9 Did you have any conversations with</p> <p>10 anyone regarding their use of other Adherus</p> <p>11 AutoSpray devices?</p> <p>12 A Would you repeat that?</p> <p>13 Q I'll rephrase it slightly. The</p> <p>14 sentence we were talking about in paragraph 35 --</p> <p>15 A Beginning with "Furthermore"?</p> <p>16 Q Exactly. Exactly. The "furthermore"</p> <p>17 sentence.</p> <p>18 This addresses -- this states, the</p> <p>19 Adherus AutoSpray Extended Tip (ET) Dural Sealant.</p> <p>20 Do you see that?</p> <p>21 A Yes.</p> <p>22 Q Now, is it your understanding that</p>	<p style="text-align: right;">Page 108</p> <p>1 statement about the colleagues you spoke with at a</p> <p>2 VCU --</p> <p>3 A Yes.</p> <p>4 Q -- this sentence is referring to the</p> <p>5 Adherus AutoSpray Extended Tip (ET) Dural Sealant?</p> <p>6 A That's correct.</p> <p>7 Q Do you see that?</p> <p>8 Did you intend to reference anyone else</p> <p>9 you spoke with regarding the three other products</p> <p>10 at issue in this case?</p> <p>11 A No, no other people.</p> <p>12 Q And in -- did you speak with anyone</p> <p>13 regarding their use of any of the three other</p> <p>14 accused products in this case other than these</p> <p>15 people listed in your reference to the AutoSpray</p> <p>16 Extended (ET) product?</p> <p>17 A Some of the conversations I had, I</p> <p>18 don't -- I didn't specify which Adherus product.</p> <p>19 I asked them more generically about the Adherus</p> <p>20 products, so -- but not all -- not -- that are not</p> <p>21 on that list, so --</p> <p>22 Q So --</p>
<p style="text-align: right;">Page 107</p> <p>1 there are other accused Adherus products in this</p> <p>2 litigation?</p> <p>3 A Yes.</p> <p>4 Q And those are the Adherus AutoSpray</p> <p>5 Dural Sealant, the Adherus Dural Sealant, the</p> <p>6 Adherus Spinal Sealant; is that correct?</p> <p>7 A Would you mind saying that list again?</p> <p>8 Q Sure. I believe if you look at</p> <p>9 paragraph 4 of your report --</p> <p>10 A Yeah.</p> <p>11 Q -- the accused products are the Adherus</p> <p>12 Spinal Sealant, the Adherus Dural Sealant, the</p> <p>13 Adherus AutoSpray Dural Sealant, and then the</p> <p>14 Adherus AutoSpray Extended Tip (ET) Dural Sealant.</p> <p>15 Do you see that?</p> <p>16 A Yes, I do, and I agree.</p> <p>17 Q And is that the -- is that the full</p> <p>18 list of your understanding of the accused products</p> <p>19 in this case?</p> <p>20 A Yes, it is.</p> <p>21 Q So going back to paragraph 30- -- 35,</p> <p>22 the thur -- thur -- thurer -- "furthermore"</p>	<p style="text-align: right;">Page 109</p> <p>1 A Is that clear?</p> <p>2 Q We can unpack that a little bit.</p> <p>3 A Okay.</p> <p>4 Q So other than the people referencing in</p> <p>5 this furth -- "furthermore" statement --</p> <p>6 A Yes --</p> <p>7 Q -- sentence --</p> <p>8 A -- sir.</p> <p>9 Q -- did you speak with anyone that</p> <p>10 informed your opinion regarding the accused</p> <p>11 products about any of the other three accused</p> <p>12 products?</p> <p>13 A It's possible I did, yes, because -- my</p> <p>14 understanding is that's our -- that's the one</p> <p>15 that's available at VCU, the Extended Tip Dural</p> <p>16 (ET), the Adherus AutoSpray Extended Tip Dural</p> <p>17 Sealant. But in the conversations, I assumed that</p> <p>18 that's what they used; it was this product. It is</p> <p>19 possible that their answers drew from the use of</p> <p>20 other Adherus products that I'm not aware of --</p> <p>21 Q Okay. So we can --</p> <p>22 A -- so --</p>

<p style="text-align: right;">Page 110</p> <p>1 Q We can get to the conversations that 2 you reference in the "furthermore" sentence in a 3 second. 4 What I'm asking is apart from the 5 conversations you're referencing in this 6 "furthermore" sentence, are there any other 7 conversations you had with individuals regarding 8 their use of the -- any of the three other accused 9 products in this case? 10 A Yes. I think I understand your 11 question. I'm attempting to answer exactly that. 12 My conversations referenced in that 13 sentence assumed that they had used this product. 14 It is possible they used the other products. We 15 didn't specify. 16 And, therefore, the answer to your 17 question would be, yes, because our conversations 18 referenced their use of the -- the 1 through 3 on 19 the list in paragraph 4. And I'm just not aware 20 of -- I didn't clarify that with them when we had 21 the conversations. 22 Q So I think we're talking past each</p>	<p style="text-align: right;">Page 112</p> <p>1 A Okay. If I misunderstood previously, 2 I'm sorry. 3 No other individuals that I can recall 4 that are not on that list did I have conversations 5 with any of the four items listed. 6 Q Okay. Thank you. 7 So moving to the individuals identified 8 in the "furthermore" sentence, it's accurate to 9 say that you might have had discussions with them 10 concerning any of the four accused products? 11 A It's possible, yes. 12 Q But in the sentence in paragraph 35, 13 you only reference the Adherus AutoSpray Extended 14 Tip (ET) Dural Sealant? 15 A Right. 16 Q And is it your opinion that HyperBranch 17 could appropriately respond to your bases for your 18 opinions stated in this report without any 19 information but what products you discussed with 20 these individuals? 21 MR. ALTHERR: Object to the form. 22 THE WITNESS: Yeah, I think I -- I have</p>
<p style="text-align: right;">Page 111</p> <p>1 other a little bit here, so we can talk to those 2 conversations here in a second. 3 Is it fair to say you have not had any 4 conversations with individuals regarding their use 5 of the three other accused products, the non-ET 6 product, other than the individuals you listed in 7 connection to the "furthermore" statement? 8 A No, I don't think that's fair because 9 it's very possible they used those three products 10 and, therefore, that conversation would have 11 concerned those three -- 12 Q Of course. 13 A -- products. 14 Q But let's -- we're going to address the 15 "furthermore" sentence and those conversations 16 with Dr. Holloway, Dr. Vega, Dr. Brzezicki, 17 Ms. Pleasants, Dr. Broaddus and the -- Steve 18 Rockwell in a minute. 19 A Yes. 20 Q Apart from these individuals, have you 21 spoken with any other individuals regarding their 22 use of the -- any of the four accused products?</p>	<p style="text-align: right;">Page 113</p> <p>1 revealed what we discussed, the products -- 2 I've -- I've mentioned the products that I believe 3 we discussed. 4 BY MR. HUGHES: 5 Q In paragraph 35 of your report, you 6 only identify the Adherus AutoSpray Extended Tip 7 (ET) Dural Sealant product; correct? 8 A That's correct. 9 Q But now you're saying you might have 10 intended to identify HyperBranch that you had 11 discussions with these individuals regarding other 12 products? 13 A That's right. Maybe it's easier to 14 just clarify that. 15 The reason I listed that product, 16 meaning number 4, the Adherus AutoSpray Extended 17 Tip Dural Sealant, is because that is my 18 understanding of the product we have available at 19 VCU. 20 I don't -- for example, two of the 21 practitioners on that list practice at another 22 hospital that I don't do surgery at, the VA</p>

<p style="text-align: right;">Page 114</p> <p>1 Medical Center in Richmond. And it's possible 2 they have used those other products to form their 3 opinion. 4 I specified this product in my expert 5 report because I -- that's my understanding of the 6 one that we're on a trial basis able to use at VCU 7 currently. 8 Q Where in your report do you state the 9 results of discussions of individuals regarding -- 10 strike that. 11 Where in your report do you identify 12 your discussions with any individuals about their 13 use of the three other Adherus products, the 14 non-ET product, that you relied upon in forming 15 your opinion? 16 A In that sentence though I don't specify 17 those other three because I'm not sure if they 18 used them. It's possible they didn't use them at 19 all. 20 Q And this is the only -- this sentence 21 in paragraph 35 that begins with "Furthermore," 22 this is the only sentence that you -- that's</p>	<p style="text-align: right;">Page 116</p> <p>1 of 2017 -- between October of 2016 and I would 2 estimate July of 2017. 3 Q And were you retained in this case in 4 July of 2017? 5 A I don't recall the exact date I was 6 retained. 7 Q Did you have discussions with 8 Dr. Holloway after you were contacted by Integra 9 in regards to this litigation? 10 A I don't believe so, no. 11 Q So there were no discussions that you 12 intended to reference for paragraph 35 of 13 Dr. Holloway that occurred after Integra contacted 14 you for this litigation? 15 A That's correct. I believe some of the 16 conversations do -- did occur after I was 17 retained, but certainly the dates -- like October, 18 the prior fall, I remember discussing this -- the 19 product. 20 Q You said some of the discussions, but 21 for Dr. Holloway, not -- 22 A Correct. With Dr. Holloway. I'll be</p>
<p style="text-align: right;">Page 115</p> <p>1 contained in your report that you identify any 2 discussions with individuals regarding any of the 3 four accused products? 4 A That's correct. It's the only sentence 5 that summarizes discussions regarding Adherus 6 products. 7 Q Okay. Now, you mentioned a second ago 8 two of the doctors on the list work at another 9 facility. Which facility is that? 10 A The VA Medical Center in Richmond, 11 Virginia. 12 Q And which two doctors is that? Which 13 two doctors from the list -- 14 A Dr. Broaddus and Holloway. 15 Q And they also perform surgeries at VCU? 16 A Correct. 17 Q So Dr. Holloway, when did you -- 18 what -- when did you have the discussions you 19 reference in paragraph 35 with Dr. Holloway? 20 A In the spring of 2017. 21 Q Approximately -- 22 A Between the fall of 2016 and the spring</p>	<p style="text-align: right;">Page 117</p> <p>1 specific. 2 Q And did -- when I say discussions 3 and -- for this conversation we're having right 4 now I'll mean in-person discussions or telephone 5 or email discussions. 6 Do you understand that? 7 A I do. 8 Q And approximately how many times did 9 you do -- have discussions with Dr. Holloway 10 regarding the ET product? 11 A I don't recall exactly. Several times. 12 Q Approximately -- 13 A Under five. 14 Q Under five? 15 A (Witness nods head.) 16 Q And what did you discuss with 17 Dr. Holloway? 18 A Her impressions of the product. 19 Q What were her impressions of the 20 product? 21 A She had used it and found it to be 22 extremely similar to the DuraSeal products but a</p>

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1 different color.

2 **Q Did she ever discuss the AutoSpray**

3 **applicator?**

4 A We did not discuss the applicator --

5 no, I did -- I take that back. I do believe I

6 discussed the applicator. I can't say with

7 certainty it was with Dr. Holloway or not.

8 **Q So we're going to go through each one**

9 **of the people --**

10 A Okay.

11 **Q -- that you've allegedly talked to --**

12 A Sure.

13 **Q -- so --**

14 A Okay.

15 **Q -- let's --**

16 A It's possible I discussed the

17 applicator with Dr. Holloway.

18 **Q Possible?**

19 A Yes.

20 **Q Do you -- do you recall what those**

21 **discussions concerning the applicator entailed?**

22 A She does a lot of transsphenoidal

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1 surgeries, so it was specific to how it performed

2 in the transsphenoidal operations.

3 **Q And as of you submitting this report**

4 **in -- August 24 of 2017, what discussions with**

5 **Dr. Holloway regarding the applicator were you**

6 **taking into account when you formed your opinion?**

7 A All of them.

8 **Q So what -- specifically what**

9 **discussions regarding the applicator were you**

10 **taking into account with Dr. Holloway?**

11 A Any discussions I have with

12 Dr. Holloway regarding her experience with Adherus

13 factors into my opinion on it.

14 **Q So I'm asking for the facts of what you**

15 **discussed with her regarding the applicator that**

16 **you took into account when you formed your opinion**

17 **and --**

18 A Oh.

19 **Q -- what are those facts.**

20 A Had she used it and what her

21 experience -- what her impression of the

22 applicator and the product were.

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1 **Q And the full scope of what you took**

2 **into account on her impression of the applicator**

3 **was that it was extremely similar to DuraSeal yet**

4 **a different color?**

5 A The product was similar to DuraSeal but

6 a different color, and the applicator had been

7 effective in her -- in -- when she used it.

8 **Q The Adherus applicator had been**

9 **effective?**

10 A That's correct.

11 **Q Did she mention any differences between**

12 **the Adherus applicator and the DuraSeal**

13 **applicator?**

14 A I don't recall her mentioning any

15 difference between the two applicators.

16 **Q Did she make any indications that she**

17 **thought the Adherus applicator was beneficial?**

18 A I don't recall her saying that.

19 **Q Did she mention any advantages or**

20 **distinctions of the Adherus applicator?**

21 A I don't recall any advantages or

22 distinctions, I believe, is what you said.

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1 **Q Did she provide any statements to you**

2 **regarding the ability to start and stop the**

3 **Adherus product during application compared to a**

4 **DuraSeal product?**

5 A No.

6 **Q Did she indicate any opinions on the**

7 **biocompatibility of the two different products --**

8 A No.

9 **Q -- of the Adherus versus DuraSeal**

10 **product?**

11 A No.

12 **Q So the full scope of the issues you're**

13 **relying upon with your discussions with**

14 **Dr. Holloway was that it was extremely similar to**

15 **the DuraSeal product yet a different color; is**

16 **that accurate?**

17 A I think that's one sentence in this.

18 Certainly the conversation was longer than one

19 sentence so I don't think it's accurate to say

20 that was the full scope.

21 I'm summarizing her impressions of

22 her -- you know, how she experienced the product,

<p style="text-align: right;">Page 122</p> <p>1 what did she think of it. And it was longer -- it</p> <p>2 was a longer conversation than that one sentence.</p> <p>3 Q So what is the full scope of your</p> <p>4 conversations with Dr. Holloway that you took into</p> <p>5 account when forming your opinion?</p> <p>6 MR. ALTHERR: Object to the form.</p> <p>7 THE WITNESS: The full -- everything</p> <p>8 she -- everything we discussed I took into</p> <p>9 account, and I think I've summarized that. She</p> <p>10 was -- it was available to her. She had used it.</p> <p>11 She had used it in transsphenoidal surgeries and</p> <p>12 found it effective and very similar to DuraSeal.</p> <p>13 We talked about the color.</p> <p>14 That's how I would summarize the scope</p> <p>15 of the conversation.</p> <p>16 BY MR. HUGHES:</p> <p>17 Q In this time frame of your discussions</p> <p>18 with her in the fall of 2016 -- October 2016</p> <p>19 through approximately July of 2017, how many times</p> <p>20 had she used the product in that period?</p> <p>21 A I don't know.</p> <p>22 Q And are there any other statements she</p>	<p style="text-align: right;">Page 124</p> <p>1 Q Okay. And --</p> <p>2 A And, again, the rationale for listing</p> <p>3 the specific product in paragraph 35 was because I</p> <p>4 believed and believe that's the one that we have</p> <p>5 available at VCU; therefore, the assumption that's</p> <p>6 the product that was utilized.</p> <p>7 Can I confirm that 100 percent? No.</p> <p>8 For example, I did not review the patients'</p> <p>9 medical records that they utilized it in.</p> <p>10 Q So you didn't review any patient's</p> <p>11 medical records where the Adherus product was used</p> <p>12 at VCU?</p> <p>13 A That's right.</p> <p>14 Q And is it fair to say you didn't review</p> <p>15 any of the patient records where an Adherus</p> <p>16 product was used at the VA hospital?</p> <p>17 A Definitely. That's true. In fact, I</p> <p>18 stated earlier I'm not sure that they used the</p> <p>19 Adherus product at the VA. I stated the VA is</p> <p>20 another hospital where they practice; that I don't</p> <p>21 know if they have access to it. They very well</p> <p>22 could, and it may have formed their opinion.</p>
<p style="text-align: right;">Page 123</p> <p>1 made regarding the product that you took into</p> <p>2 account when you formed your opinion other than</p> <p>3 what you just stated?</p> <p>4 A Not that I can recall.</p> <p>5 Q So you're saying you summarized the</p> <p>6 opinion, but there aren't any other specific facts</p> <p>7 of your discussions with her that you took into</p> <p>8 account?</p> <p>9 A Not that I can recall, that's correct.</p> <p>10 Q And those discussions would have</p> <p>11 involved her work both at VCU and the VA hospital?</p> <p>12 A I assume so. When she answered the</p> <p>13 question, I certainly can't speak to what formed</p> <p>14 her answer, but I assumed so.</p> <p>15 Q Did she reference using any of the</p> <p>16 other four accused products other than the ET</p> <p>17 product?</p> <p>18 A Not that I recall. I think I've --</p> <p>19 I've stated, and I'll restate, during our --</p> <p>20 during the conversations I had with that list of</p> <p>21 people, I did not specify which of the four</p> <p>22 accused products they had used.</p>	<p style="text-align: right;">Page 125</p> <p>1 Q Okay.</p> <p>2 A And it -- it isn't listed. That was</p> <p>3 the reason for --</p> <p>4 Q I -- I understand.</p> <p>5 But you're not -- you're not aware of</p> <p>6 the VA hospital's use of any Adherus product --</p> <p>7 any of the four accused Adherus products?</p> <p>8 A That is correct.</p> <p>9 Q And Dr. Vega, who is Dr. Vega?</p> <p>10 A One of the neurosurgery residents.</p> <p>11 Q One of the --</p> <p>12 A Resident physicians.</p> <p>13 Q And when did you talk to Dr. Vega?</p> <p>14 A Same time period, October 2016 through</p> <p>15 July of 2017.</p> <p>16 Q Did you talk to Dr. Vega about the</p> <p>17 Adherus product that you identify in paragraph 35</p> <p>18 of your report after you were retained by Integra</p> <p>19 in this litigation?</p> <p>20 A Two things to clarify. Your question,</p> <p>21 you said that I mentioned in the report. Again</p> <p>22 I'll say I did not specify this device in the</p>

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1 conversations with them. I only referenced
 2 Adherus products, number one.
 3 Number two, the -- it is -- I don't
 4 recall the exact dates of these conversations, and
 5 the time period includes both before I was
 6 retained and after.
 7 **Q Okay. Let's step back with**
 8 **Dr. Holloway. So the discussions with**
 9 **Dr. Holloway occurred both before and after you**
 10 **were retained as an expert in this case?**
 11 A I can't recall the exact dates, so,
 12 yes, I believe they could have occurred before or
 13 after. It was during this time period that I
 14 became aware of the product being available, and I
 15 don't know the exact dates. I didn't make a
 16 record.
 17 **Q Were you retained in this litigation**
 18 **prior to July of 2017?**
 19 A Yes.
 20 **Q Were you retained in this litigation**
 21 **prior to June of 2017?**
 22 A I don't recall the exact dates, but I

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1 believe so, yes.
 2 **Q And you said it was the spring of 2017**
 3 **that you first had interaction with Chris Roth**
 4 **from the Banner Witcoff firm; is that accurate?**
 5 A Yes, and I can -- I recall more
 6 specifically that -- I know why I had the
 7 interaction with Steve --
 8 That's who you asked about; is that
 9 correct? Is that the -- Rockwell -- is that the
 10 name you just said?
 11 **Q No, I said Chris Roth at the --**
 12 A Oh, I beg your --
 13 **Q -- Banner --**
 14 A -- pardon.
 15 **Q -- Witcoff --**
 16 A I'm sorry. Would you repeat it, then,
 17 just for clarity?
 18 **Q Sure.**
 19 **It was the spring of 2017 that you**
 20 **first had interaction with the Banner & Witcoff**
 21 **firm; is that --**
 22 A Yes.

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1 **Q -- accurate?**
 2 A Correct.
 3 **Q But you don't recall if you were**
 4 **retained by June of 2017 or not?**
 5 A I believe I was, but I don't recall the
 6 exact dates. Certainly that's a date we could
 7 find.
 8 **Q Well, for the purpose of our discussion**
 9 **today, is that something you could find by the end**
 10 **of the day?**
 11 A Yes, I believe it is.
 12 **Q Okay. So I'll ask you to try -- on the**
 13 **next break try to determine the date that you were**
 14 **retained by the Banner & Witcoff firm?**
 15 A Understood.
 16 **Q Did anyone from Banner & Witcoff ask**
 17 **you to talk to any of the surgeons that you**
 18 **reference in paragraph 35 regarding the use of the**
 19 **ET product?**
 20 A No, not that I recall.
 21 **Q Did anyone at the Banner Witcoff firm**
 22 **ask you to discuss this with Ms. Pleasants?**

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1 A No.
 2 **Q And that was both before and after you**
 3 **were retained in this litigation?**
 4 A I believe Ms. -- the conversa- -- no,
 5 I -- I -- I can more exactly specify when the
 6 conversation with Ms. Pleasants occurred because
 7 it was a -- I had a conversation to attempt to use
 8 the product, and I asked her to arrange for that.
 9 **Q So you had a conversation to attempt to**
 10 **use the product. Which product are you referring**
 11 **to?**
 12 A The Adherus AutoSpray Dural Sealant.
 13 **Q And when was that conversation?**
 14 A I believe it was either -- it was
 15 between May and July of 2017. I know the case. I
 16 could -- I could find the exact date at another
 17 time but not today, but I know the patient I
 18 wanted to use it on and I could recall -- I could
 19 find that date.
 20 **Q What type of procedure was that?**
 21 A It was a craniotomy.
 22 **Q Craniotomy.**

<p style="text-align: right;">Page 130</p> <p>1 And is there a difference between the 2 ET product and the -- what I'll call the regular 3 Adherus AutoSpray product for use in a craniotomy? 4 A I don't -- I don't know the answer to 5 that question. 6 Q So you testified it was somewhere 7 around May or July of 2017 that you asked 8 Ms. Pleasants to attempt to obtain the ET product 9 for use in a case? 10 A Correct. 11 Q When I say "case," I mean surgical 12 procedure. 13 And why -- 14 A Understood. And, yes. 15 Q Why did you ask Ms. Pleasants to try to 16 obtain the ET product for you? 17 A Because I was interested in using it. 18 Q Why were you interested in using it? 19 A So we have a process where new products 20 are trialed at VCU where we have the opportunity 21 to decide is it something we want to keep -- stock 22 regularly at the hospital.</p>	<p style="text-align: right;">Page 132</p> <p>1 was retained. 2 THE WITNESS: I was going to say -- 3 MR. ALTHERR: Anything -- any- -- 4 THE WITNESS: -- he just -- 5 MR. ALTHERR: -- -thing -- 6 THE WITNESS: -- asked when -- 7 MR. ALTHERR: -- before -- 8 THE WITNESS: -- I was -- 9 MR. ALTHERR: -- he -- 10 THE WITNESS: -- retained. 11 MR. ALTHERR: -- was retained. 12 MR. HUGHES: So your position, Counsel, 13 so we're clear, is that any discussions regarding 14 Dr. Rivet seeking to use the ET product after he 15 was retained as work product, and those 16 discussions he should not answer -- should not 17 respond to in this -- 18 MR. ALTHERR: No, that's not what I 19 said. I said any discussions, period, that we had 20 after he was retained are privileged, all right? 21 And that's what my objection is, okay? 22 MR. HUGHES: Okay.</p>
<p style="text-align: right;">Page 131</p> <p>1 And I had heard about the product from 2 my colleagues. I knew that it was available, and 3 I wanted to try it on a particular case to have 4 more experience with it and compare it to the 5 DuraSeal product. 6 Q And when you sought to use the ET 7 product, had you been retained in this case at 8 that time? 9 A Yes. 10 Q And did your interest in using the ET 11 product have anything to do with your retention in 12 this litigation? 13 A I thought it would further inform my 14 opinion. 15 Q Did you discuss your potential use of 16 the ET product with counsel in this litigation? 17 MR. ALTHERR: Object to form. As a 18 matter of fact, I'm going to instruct the witness 19 not to answer that. Anything he discussed with us 20 would be work product. 21 MR. HUGHES: So you're instructing -- 22 MR. ALTHERR: After he was -- after he</p>	<p style="text-align: right;">Page 133</p> <p>1 MR. ALTHERR: Any restr- -- any -- any 2 discussions, period. 3 MR. HUGHES: And that's you're 4 instruction to the witness, not to testify on. 5 MR. ALTHERR: That's right. That's 6 work product and -- once he was retained, okay? 7 MR. HUGHES: Okay. 8 BY MR. HUGHES: 9 Q So, Dr. Rivet, you mentioned that you 10 thought using the ET product would further inform 11 your engagement in this litigation; is that 12 accurate? 13 MR. ALTHERR: Object to the form. 14 THE WITNESS: Among other things, yes. 15 I'm interested in using it clinically. It's a new 16 product. We trial products all the time. 17 BY MR. HUGHES: 18 Q But you also were interested in using 19 it due to your involvement in this litigation; is 20 that accurate? 21 A Yes. 22 Q Did you end up using the ET product?</p>

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1 A I did not.

2 **Q Have you ever used the ET product?**

3 A I have not.

4 **Q Have you ever used any Adherus product?**

5 A No.

6 **Q Why did you not use the ET product?**

7 A I was prevented from using it.

8 **Q Was that -- and is it accurate -- is it**

9 **fair to say that you thought the ET product would**

10 **be beneficial for your patient?**

11 A Yes.

12 **Q Was that the first time that you**

13 **considered using the ET product on a patient?**

14 A No.

15 **Q When was the first time that you**

16 **considered using the ET product on a patient?**

17 A As soon as I heard about it being

18 available.

19 **Q When was that?**

20 A Some -- as I -- sometime between

21 October of 2016 and -- and the spring of 2017.

22 **Q Did you ever decline to use the ET**

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1 **product when offered to you?**

2 A No. It was the opposite.

3 **Q That you --**

4 A I re- --

5 **Q -- sought --**

6 A I re- --

7 **Q -- to --**

8 A Correct. I requested to use the

9 product and was denied the ability to use it.

10 **Q And that was in May/June of 2017?**

11 A Approximately, yes.

12 **Q After you were retained as an expert**

13 **witness for Integra in this litigation?**

14 A Correct.

15 **Q You mentioned Steve Rockwell. Is he**

16 **the sales rep for Adherus?**

17 A I believe he's either the sales rep or

18 the distributor, that's right.

19 **Q Okay. And have you ever spoken to**

20 **Steve Rockwell regarding your use of an Adherus**

21 **product?**

22 A Yes. He mentioned the fact that it was

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1 available and told me about the product.

2 **Q And when was that?**

3 A Same time period. Between -- sometime

4 between October 2016 and July of 2017.

5 **Q How many times did you speak with Steve**

6 **Rockwell regarding potential use of the product**

7 **between October 2016 and July 2017?**

8 A Several times. One to three times,

9 approximately.

10 **Q And these were in-person communications**

11 **or emails?**

12 A In-person communications. There may

13 have been a -- he may have -- I may have talked to

14 him on the phone as well. Either in person or on

15 the telephone. I don't recall exactly which.

16 **Q Okay. And did Steve Rockwell ever --**

17 **ever offer to provide you with the ET product for**

18 **your use?**

19 A Yes.

20 **Q When was that?**

21 A I don't recall the exact date. It

22 was -- in our initial conversation, he explained

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1 that it was available for use, and that was an

2 offer to make it available to come in for the

3 case, et cetera.

4 **Q And that was sometime between 2000 --**

5 **October of 2016 and July of 2017, but you can't**

6 **remember when; is that accurate?**

7 A Correct. That's right.

8 **Q Was that -- the first time you spoke**

9 **with Steve Rockwell where he offered you to use**

10 **the ET product, was that before or after you were**

11 **engaged in this litigation?**

12 A Before.

13 **Q What was your response to Steve**

14 **Rockwell when he offered that you could use the ET**

15 **product?**

16 A Positive. I said I would consider it

17 and look for a case I thought that was

18 appropriate; that I had heard about the case --

19 that I had heard about the product and was

20 interested in -- in trying it.

21 **Q Did you ever indicate to Steve Rockwell**

22 **that you could not use the ET product due to a**

<p style="text-align: right;">Page 138</p> <p>1 conflict?</p> <p>2 A Yes.</p> <p>3 Q When was that?</p> <p>4 A I -- I don't recall the exact date.</p> <p>5 Q Was that in July of 2017?</p> <p>6 A It may have been.</p> <p>7 Q So at the same time you're requesting</p> <p>8 to use the ET product, you said to Steve you could</p> <p>9 not use it because you had a conflict?</p> <p>10 MR. ALTHERR: Object to the form.</p> <p>11 THE WITNESS: No, that's not correct.</p> <p>12 BY MR. HUGHES:</p> <p>13 Q Well, you just testified that around</p> <p>14 July 2017 you sought to use the ET product; is</p> <p>15 that accurate?</p> <p>16 A Correct.</p> <p>17 Q But then you also said, in July of</p> <p>18 2017, you told Steve Rockwell you could not use</p> <p>19 the product because you have a conflict --</p> <p>20 A No.</p> <p>21 Q -- is that accurate?</p> <p>22 A No, that's not.</p>	<p style="text-align: right;">Page 140</p> <p>1 A Correct.</p> <p>2 Q Okay.</p> <p>3 MR. HUGHES: The videographer -- the</p> <p>4 videographer has indicated the tape is about to</p> <p>5 end. So can we go off the record?</p> <p>6 THE VIDEOGRAPHER: This concludes disk</p> <p>7 number 1 of the video deposition of Dennis Rivet,</p> <p>8 M.D. The time is 11:16:06 a.m. We are now off</p> <p>9 the record.</p> <p>10 (Recess -- 11:16 a.m.)</p> <p>11 (After recess -- 11:20 a.m.)</p> <p>12 (Written record only.)</p> <p>13 MR. ALTHERR: Can you read back the</p> <p>14 last question and answer?</p> <p>15 (The Record was read as requested.)</p> <p>16 THE VIDEOGRAPHER: This begins disk</p> <p>17 number 2 of the video deposition of Dennis Rivet,</p> <p>18 M.D. The time is approximately 11:20:10 a.m.</p> <p>19 We're now on the record.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q Dr. Rivet, were you by chance able to</p> <p>22 confirm when you were retained in this litigation</p>
<p style="text-align: right;">Page 139</p> <p>1 Q Okay.</p> <p>2 A The July 2017 is not. So I had heard</p> <p>3 about the product -- I had had a conversation or</p> <p>4 conversations with him about the availability of</p> <p>5 it; that I was interested in using it. And then</p> <p>6 later -- and I don't recall the exact date -- I --</p> <p>7 I said to him that I may have a conflict and I</p> <p>8 would look into that.</p> <p>9 And I don't recall the date of that</p> <p>10 conversation exactly.</p> <p>11 Q Would -- that conversation would have</p> <p>12 occurred after you were retained in this</p> <p>13 litigation?</p> <p>14 A Correct.</p> <p>15 Q And did you decline to use the product</p> <p>16 at that time due to your engagement in this</p> <p>17 litigation?</p> <p>18 A No, I did not decline to use the</p> <p>19 product at any point.</p> <p>20 Q So when you indicated to Steve Rockwell</p> <p>21 that you might have a conflict, you did not</p> <p>22 decline to use the product at that time?</p>	<p style="text-align: right;">Page 141</p> <p>1 during the break?</p> <p>2 A No.</p> <p>3 Q Before the break, we were discussing</p> <p>4 your discussions with Steve Rockwell regarding the</p> <p>5 Adherus ET product.</p> <p>6 Do you remember that?</p> <p>7 A (Witness nods head.)</p> <p>8 Q And you testified that you spoke with</p> <p>9 Mr. Rockwell one to three times regarding the ET</p> <p>10 product; correct?</p> <p>11 A Yes.</p> <p>12 Q And those discussions occurred between</p> <p>13 October 2016 and July of 2017; correct?</p> <p>14 A That's my recollection, yes.</p> <p>15 Q And in July 2017, you sought to use the</p> <p>16 ET product; correct?</p> <p>17 A I've said approximately. I don't</p> <p>18 recall whether it was 100 -- I think I gave a</p> <p>19 month range, but it's possible it wasn't in July.</p> <p>20 Q And you did not use the product then;</p> <p>21 correct?</p> <p>22 A That's correct.</p>

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1 **Q But on the previous conversation with**
 2 **Mr. Rockwell, you indicated that you might have a**
 3 **conflict using the product; correct?**
 4 A Correct.
 5 **Q Was that the first discussion with**
 6 **Mr. Rockwell regarding the ET product?**
 7 A No.
 8 **Q Was that the second discussion with**
 9 **Mr. Rockwell regarding the ET product?**
 10 A I don't recall if it was the second
 11 or -- or the third. It was not the first
 12 conversation.
 13 **Q And did -- do you recall -- that**
 14 **conversation that you might have a conflict, was**
 15 **that before or after you were retained in this**
 16 **litigation?**
 17 A It would have been after I was
 18 retained.
 19 **Q And why would you have a conflict using**
 20 **the product if you were retained in this**
 21 **litigation?**
 22 MR. ALTHERR: Object to the form.

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1 THE WITNESS: I didn't --
 2 BY MR. HUGHES:
 3 **Q You didn't --**
 4 A -- have a --
 5 **Q -- have --**
 6 A -- conflict.
 7 **Q -- a conflict?**
 8 **Why would you potentially have a**
 9 **conflict using the product?**
 10 A I was not -- I questioned whether
 11 there -- there might be a reason I couldn't use
 12 the product and, therefore, wanted to review the
 13 engagement and documentation I had to see if that
 14 would be a problem.
 15 There are also -- our institution
 16 has -- the process by which we add products to the
 17 hos- -- what's available --
 18 **Q How is --**
 19 A -- there --
 20 **Q How is that relevant to the --**
 21 A I'm --
 22 **Q -- conflict?**

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1 A I'm going to explain that.
 2 **Q Okay.**
 3 A That -- that process solicits opinions
 4 from the users after they've had an attempt to
 5 trial things. And if an individual has a
 6 relationship with a company that's being
 7 trialed -- for example, they're a co-inventor;
 8 they're a stockholder; they have some interest in
 9 a product -- they're supposed to disclose that.
 10 And I wanted to review what the -- what
 11 the nature of a relationship should be during that
 12 evaluation process at VCU, and I wasn't familiar
 13 with that at the time of that -- either second or
 14 later conversation with him occurred.
 15 **Q Is Steve Rockwell a physician?**
 16 A No, not that I'm aware of.
 17 **Q And did -- did you rely on any of the**
 18 **conversations with Mr. Rockwell regarding the use**
 19 **of the Adherus AutoSpray ET product?**
 20 A Yes.
 21 **Q And now going back to paragraph 35, the**
 22 **"furthermore" sentence we've been discussing**

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1 **previously which states, I have spoken to my**
 2 **colleagues at VCU who used the Adherus AutoSpray**
 3 **Extended Tip (ET) Dural Sealant product, isn't it**
 4 **correct that earlier you testified your**
 5 **discussions with Steve Rockwell would fall within**
 6 **that sentence?**
 7 A Yes. I think -- I consider him a
 8 colleague at VCU, yes.
 9 **Q And what discussions did you have with**
 10 **Steve Rockwell that you relied upon in forming**
 11 **your opinions in this report?**
 12 A When -- the first discussion I had with
 13 him, I -- he mentioned that it was available for
 14 use and that others -- that my colleagues had used
 15 it. And I believe he referenced who had used it;
 16 although, I don't recall exactly. And as
 17 expected, he was positive. He was enthusiastic
 18 about -- as you'd expect, as he represented the
 19 company, about our trying it.
 20 **Q And did you rely upon any specific**
 21 **facts in your discussions with Mr. Rockwell in**
 22 **forming your opinion in this report?**

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1 A Just what I just stated, that others
 2 had had a favorable -- that his -- the feedback he
 3 had received had been favorable from the other
 4 surgeons.
 5 **Q At the time you signed this report on**
 6 **August 24th, 2017, approximately how many people**
 7 **who you consider your colleagues at VCU had used**
 8 **the Adherus product?**
 9 A I don't know.
 10 **Q Would it be more than ten?**
 11 A I don't know.
 12 **Q More than five?**
 13 A I -- I don't know.
 14 **Q Do you have any idea of approximately**
 15 **how many?**
 16 A Well, we only have approximately 26
 17 members of our department that are physicians that
 18 are users, so it would certainly be less than
 19 that.
 20 But I don't know. I would estimate in
 21 the range you've said is reasonable. It's
 22 possible that there are only four people; it's

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1 possible that ten people had used it.
 2 I -- I don't know the answer to that
 3 question.
 4 **Q So the range of five to ten would be a**
 5 **reasonable --**
 6 A Would be --
 7 **Q -- estimation?**
 8 A -- reasonable, yes, sir. That's
 9 correct.
 10 **Q And then do you also include nurses and**
 11 **other sales reps as your colleagues at VCU who you**
 12 **might have spoken to regarding ET Dural Sealant?**
 13 A Yes. Debbie Pleasants, for example, is
 14 a nurse.
 15 **Q You said Mr. Rockwell might have said**
 16 **more people at VCU had used the product. Do you**
 17 **remember which -- any specific people he mentioned**
 18 **who used the product?**
 19 A I don't. In fact, I'm not certain he
 20 was referring to only people at VCU. I think
 21 he -- generically, it was that the feedback he had
 22 received was positive.

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1 **Q And is it accurate to say in this**
 2 **sentence in paragraph 35, you're not referring to**
 3 **physicians at the VA hospital in Richmond other**
 4 **than the two people who also work at VCU?**
 5 A Well, the -- no, because the other
 6 people on that list also do and have worked at the
 7 VA.
 8 **Q Okay. But other than the people we**
 9 **identified in relation to the "furthermore"**
 10 **sentence, you're not relying upon anyone -- any**
 11 **conversation with people at the VA hospital; is**
 12 **that accurate?**
 13 A That are not on that list. I -- I have
 14 not relied on people who are not on that list for
 15 conversations.
 16 **Q Okay. So you mentioned Ms. Pleasants.**
 17 **Ms. Pleasants is a nurse at VCU; is that accurate?**
 18 A Correct.
 19 **Q And other than attempting to use the**
 20 **Adherus product in July of 2017, did you have any**
 21 **other discussions with Ms. Pleasants that you're**
 22 **referring to in paragraph 35 of your report?**

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1 A Can I just clarify again I -- I can't
 2 say with certainty it was July? In the first part
 3 of your sentence again --
 4 **Q Okay.**
 5 A -- you said July. If we can agree that
 6 it was a range of time over the spring and summer
 7 of 2017.
 8 But, yes, as I recall I had multiple
 9 conversations with Debbie confirming that it was
 10 available, first of all, and, again, the nature of
 11 how the use had gone.
 12 So she supervises all the nurses in the
 13 operating room; and if a new device is introduced
 14 and there was a problem immediately, she would be
 15 aware of it.
 16 **Q So your discussions with Ms. Pleasants**
 17 **that you're referring to in paragraph 35 here,**
 18 **when you signed your report in August 24 of 2017,**
 19 **extended beyond your attempt to use the ET**
 20 **product?**
 21 A Correct. I mean, if you consider
 22 confirming it was available and her impressions of

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1 what had -- you know, how it had gone and were
 2 there any problems with it up to that point,
 3 exactly.
 4 **Q So what discussions with her regarding**
 5 **the use of the ET product at VCU are you referring**
 6 **to in this sentence in paragraph 35?**
 7 A Any conversations I had with her.
 8 **Q Approximately how many conversations**
 9 **did you have with her regarding the use of the ET**
 10 **product at VCU?**
 11 A Two to three conversations.
 12 **Q And were those in person or over email?**
 13 A They could have been over -- either by
 14 telephone or in person. I don't recall emailing
 15 her about it -- strike that.
 16 I do -- I may have emailed her as a
 17 request to use the product, so the communications
 18 could have been in any of the forms you mentioned.
 19 **Q And these communications, did they all**
 20 **occur after you were retained in this litigation?**
 21 A I don't re- -- I don't recall.
 22 **Q But at least some of them occurred**

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1 **after you were retained in this litigation; is --**
 2 A Correct.
 3 **Q -- that correct?**
 4 A As we've discussed, yes.
 5 **Q Specifically what facts did you rely**
 6 **upon -- that you identify here in paragraph 35 --**
 7 **in forming your opinion from your discussions with**
 8 **Ms. Pleasants regarding the use of the ET product?**
 9 A Yeah. The fact -- confirming it had
 10 been used and were there -- were there impressions
 11 that she had gained from people that had used it,
 12 and I would include her nursing staff, the people
 13 in the operating room, as well as the physicians
 14 who give her feedback.
 15 Were there problems identified?
 16 Basically, was there a reason I should consider
 17 not using it. Did she know of a reason it
 18 wouldn't be a good idea, for example. Had she
 19 received feedback that the device had failed or
 20 something like that.
 21 **Q Did she provide you with any reasons**
 22 **why you should not use the product?**

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1 A She did not.
 2 **Q Did she give you any reasons why you**
 3 **may want to use the Adherus product?**
 4 A Only in that it was -- it was in that
 5 period of time where we trialed devices, so if no
 6 one uses the devices, then we don't -- nothing
 7 happens in that process.
 8 So she makes us aware of things being
 9 available so that we can use them and form an
 10 opinion, and they can make a decision.
 11 **Q As a matter of clarity for terminology,**
 12 **a device -- you're referring to a device as just**
 13 **something that doesn't go into the human body?**
 14 A I -- I would say, broadly, we trialed
 15 not just implantable devices, but we also trial
 16 things that are instruments.
 17 And again that would come from Debbie,
 18 so I would mean it in both contexts.
 19 **Q Okay. So with your discussions with**
 20 **Ms. Pleasants, did she express any indication**
 21 **regarding the applicator of the Adherus ET**
 22 **product?**

Page 153

1 A No -- she mentioned that we had one
 2 on-site. She mentioned that we have it in -- in
 3 the building. It didn't -- you know, it was
 4 available on short order.
 5 **Q Did she -- you -- you -- you testified**
 6 **that she speaks for other nurses and other people**
 7 **at VCU who may have used the ET product.**
 8 **Did she convey to you any facts**
 9 **regarding the use of the ET product from these**
 10 **other individuals?**
 11 A Only that there hadn't -- she did not
 12 know of any problems with it.
 13 **Q Did she mention any potential**
 14 **benefits --**
 15 A She did not.
 16 **Q -- of the product?**
 17 A She did not.
 18 **Q So other than that it was available in**
 19 **the -- at VCU, that there were no other problems**
 20 **with the use of the ET product, are there any**
 21 **other facts from Ms. Pleasants that you obtained**
 22 **that you relied upon in your opinion?**

Page 154

1 A Not that we haven't discussed.

2 **Q And were there any other opinions of**

3 **Ms. Pleasants that you relied upon in forming your**

4 **opinion other than it was available at VCU and**

5 **that people had generally good experiences with**

6 **the device?**

7 A No.

8 **Q Between the first time that you told**

9 **Mr. Rockwell you may have conflict using the ET**

10 **device and the time you requested to use the ET**

11 **device, how long of a time elapsed between those**

12 **two -- those two events?**

13 A I would estimate several months.

14 **Q Several months.**

15 A In the order of two to four months

16 would be my estimate.

17 **Q And during that time frame, did you**

18 **ever request to use the ET product?**

19 A My -- well --

20 **Q Before you requested and you weren't**

21 **able to use it.**

22 A No. I think if I understand your

Page 155

1 question, I -- I made a single request to use it.

2 **Q Okay. And it had never been -- you had**

3 **never considered it to use in a patient before**

4 **your single request to use it?**

5 A No, that's not accurate.

6 **Q Did you request from Mr. Rock- --**

7 **strike that.**

8 **After you told Mr. Rockwell you might**

9 **have a conflict using the product, did you follow**

10 **up with him on whether you had a conflict or not?**

11 A I don't -- I don't recall following up

12 with him directly.

13 **Q Did you follow up with anyone -- did**

14 **you follow up with him indirectly?**

15 A Yes. When I requested to use the

16 product, I had confirmed that -- to my

17 satisfaction I didn't have a conflict.

18 **Q And how did you confirm to your**

19 **satisfaction you did not have a conflict?**

20 A So I reviewed the literature -- I

21 reviewed the contract, the agreement with Banner

22 Witcoff, and I reviewed the policy at VCU

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1 regarding the evaluation of devices, this process.

2 **Q Going back to the people you just --**

3 **you were implicitly referencing in paragraph 35 in**

4 **your "furthermore" statement, we started talking**

5 **about Dr. Vega.**

6 **Is it accurate he's a resident at VCU?**

7 A Yes.

8 **Q And you previously testified that you**

9 **had spoken with him regarding the use of the ET**

10 **product between October 2016 and July of 2017?**

11 A Correct.

12 **Q Approximately how many times did you**

13 **speak with Dr. Vega in that period?**

14 A One or two times.

15 **Q And were those discussions before or**

16 **after you were retained in this litigation?**

17 A I don't recall.

18 **Q Is it fair to say that those**

19 **litigations -- those discussions could have**

20 **happened after you were retained in the**

21 **litigation?**

22 MR. ALTHERR: Object to the form.

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1 THE WITNESS: Yes.

2 BY MR. HUGHES:

3 **Q And were these email discussions or**

4 **in-person discussions?**

5 A In person.

6 **Q And what did -- what facts did you rely**

7 **upon in forming your opinion for -- in your report**

8 **based upon your discussions with Dr. Vega?**

9 A Again his impressions. You know, I

10 asked him had he used it, had he been involved in

11 a case where it was used, and what did he think of

12 it.

13 **Q And what facts or opinions that**

14 **Mr. Vega shared with you that you relied upon in**

15 **your opinion regarding whether he used it or not?**

16 **Specifically what did you rely upon from Mr. Vega?**

17 MR. ALTHERR: Object to the form.

18 THE WITNESS: Him -- his answers to --

19 him -- his impressions of the device; had he --

20 what did he experience; was it effective --

21 BY MR. HUGHES:

22 **Q Had he --**

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1 A -- et cetera.

2 **Q -- used the device?**

3 A Yes, he was involved -- he said he was

4 involved in cases where the -- it was used.

5 **Q Approximately how many cases?**

6 A I didn't ask him. I don't recall

7 asking him, anyway.

8 **Q So the number of times that he had used**

9 **the ET product did not -- strike that.**

10 **You did not consider the number of**

11 **times Dr. Vega had used the ET product when**

12 **forming your opinion identified in paragraph 35 of**

13 **your report; correct?**

14 A No. I knew that all the physicians had

15 a limited experience at VCU. This is on a trial

16 period.

17 **Q And did you discuss any of the other**

18 **accused products with Dr. Vega?**

19 A I think this is something we've --

20 we've touched on, so I believe it's possible that

21 he used one of the other products, and I didn't

22 specify which product from Adherus he used.

Page 159

1 **Q Okay. And did he -- what --**

2 **specifically what did he tell you about the use of**

3 **the product that you relied upon in forming your**

4 **opinion?**

5 A That he used it; that it was favorable.

6 We talked about the difference in color.

7 **Q What about the difference in color did**

8 **he -- did you rely upon based on your conversation**

9 **with him?**

10 A He recalled the difference in the

11 product being green, not blue. I think it's --

12 it's -- it's a thing that easily recalls from

13 memory the difference between the two products,

14 and he easily recalled the -- having used it from

15 the color. It seemed to me he easily recalled

16 it -- recalled using it.

17 **Q Did you discuss the use of the ET**

18 **applicator with Dr. Vega?**

19 A I didn't -- I don't remember

20 specifically discussing the applicator with him.

21 **Q Do you remember anything favorable he**

22 **might have said about the Adherus product in**

Page 160

1 **general?**

2 A That it was effective; that he had

3 no -- he had no negative impressions of it during

4 our conversation.

5 **Q Did he express any opinion regarding**

6 **the benefits of its application, how easily it is**

7 **applied compared to the DuraSeal product?**

8 MR. ALTHERR: Object to the form.

9 THE WITNESS: I don't recall that, no.

10 BY MR. HUGHES:

11 **Q And Dr. Brzezicki, who is**

12 **Dr. Brzezicki?**

13 A He was a neurosurgery resident as well

14 at VCU.

15 **Q He was. Is he no longer at VCU?**

16 A That's correct.

17 **Q And when did you -- approximately how**

18 **many times did you speak with Dr. Brzezicki**

19 **regarding the use of the ET product that you**

20 **relied upon in paragraph 35 of your report?**

21 A Again I think possibly just a single

22 time, one or two times.

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1 **Q And when were those conversations?**

2 A Same time period.

3 **Q October of 2016 to July of 2017?**

4 A Correct.

5 **Q And were those conversations before or**

6 **after you were retained in this litigation?**

7 A I -- I don't recall. They certainly

8 could have been either. Same time period -- that

9 time period we just discussed, October through

10 July, overlaps when I believe I was retained.

11 **Q And what specific facts or opinions**

12 **from Dr. Brzezicki were you relying upon when you**

13 **formed your opinion in paragraph 35?**

14 A Same as my conversations with the other

15 providers. Had they -- had they used it and what

16 were their impressions of its ease of use and its

17 effectiveness as a dural sealant.

18 Again, the color came up.

19 **Q When you say "the color," it was --**

20 **that it was the color green versus the color blue?**

21 A Correct.

22 **Q Anything else with the color came up?**

Page 162

1 A Not that I recall.

2 **Q And referring to your discussions with**

3 **Dr. Vega, did anything else come up regarding**

4 **color with Dr. Vega other than it was a green**

5 **color versus DuraSeal's blue color?**

6 A Not that I recall.

7 **Q Regarding color in your discussions**

8 **with Dr. Holloway, did any discussions of color**

9 **other than Adherus' green versus DuraSeal's**

10 **blue -- did you discuss any of those issues with**

11 **her?**

12 A I don't recall her -- other than the

13 difference of color.

14 **Q And the difference of color, that**

15 **Adherus is green where DuraSeal is blue --**

16 A Correct.

17 **Q -- correct?**

18 **Did Dr. Brzezicki discuss any benefits**

19 **of Adherus with you?**

20 A My recollection of the conversation

21 with him was that he was also favorably impressed

22 with its -- its use.

Page 163

1 **Q And favorably impressed compared to**

2 **DuraSeal?**

3 A That it was as effective.

4 **Q Did he mention any benefits of the**

5 **Adherus product over DuraSeal?**

6 A No --

7 MR. ALTHERR: Object to --

8 THE WITNESS: -- not --

9 MR. ALTHERR: -- form.

10 THE WITNESS: -- that I recall.

11 BY MR. HUGHES:

12 **Q And Dr. Broaddus -- I'm sorry, the**

13 **name --**

14 A Broaddus.

15 **Q Broaddus?**

16 A Uh-huh.

17 **Q How many times did you speak with**

18 **Dr. Broaddus regarding the ET product that you**

19 **reference in paragraph 35 of your report?**

20 A Same thing. A small number of times.

21 And, as I recall, Dr. Broaddus -- what I'm

22 recollect -- he discussed it with the department

Page 164

1 as a whole during one of our conferences. The use

2 of it had come up.

3 That wasn't an individual discussion I

4 had with him. It was a -- you know, a group

5 discussion.

6 **Q So did he give a presentation of some**

7 **sort to the --**

8 A He --

9 **Q -- group?**

10 A -- did not.

11 **Q But it was a discussion with the group**

12 **in general that he had?**

13 A Correct. We were discussing the fact

14 that it was available, and I believe, as I recall,

15 he had used it in a transsphenoidal case.

16 **Q Did you have any other conversations**

17 **than this group conversation with Dr. Broaddus**

18 **regarding the use of the ET product?**

19 A I believe I did have another

20 conversation about his impression of it in that

21 case and others regarding his, you know,

22 impression: Did it work as effectively? Was he

Page 165

1 happy with it?

2 These are --

3 **Q Uhm --**

4 A Go ahead. Excuse me.

5 **Q I'm sorry. Finish --**

6 A These --

7 **Q -- your --**

8 A These --

9 **Q -- answer.**

10 A These conversations are conversations I

11 would typically have prior to using a new device.

12 It's nice to solicit other colleague's impression

13 of how it work prior to using it for the first

14 time.

15 And, typically, we don't trial that

16 many products at VCU, so --

17 **Q Is it fair to say you spoke with**

18 **Dr. Broaddus one or two times regarding the ET**

19 **product?**

20 A Yes.

21 **Q And --**

22 A I'm sorry. Can I again specify? You

Page 166

1 said "the ET product." I -- during my
 2 conversations, we certainly didn't -- he didn't
 3 specify that it was the ET product. It was a more
 4 generic discussion regarding Adherus products.
 5 **Q But in your report on paragraph 35, the**
 6 **ET product is the only product you identify in**
 7 **your report, though; is --**
 8 A Correct.
 9 **Q -- that correct?**
 10 A And we've covered why.
 11 **Q Yeah.**
 12 **The discussion -- the one to two**
 13 **discussions with Dr. Broaddus, what specific facts**
 14 **or opinions of his did you rely upon in forming**
 15 **your opinion in paragraph 35?**
 16 A That he had used it in skull-based
 17 cases and transsphenoidal. That he was
 18 favorable -- favorably inclined to use it. He
 19 liked it.
 20 **Q Why did he like it?**
 21 A I think its ease of use; it performs
 22 similarly.

Page 167

1 **Q What are -- what were the ease of use**
 2 **that he communicated to you?**
 3 A He did not.
 4 **Q But he indicated that there was a --**
 5 **the Adherus product was easy to use?**
 6 A Correct.
 7 **Q Did he discuss the ease of use of the**
 8 **Adherus product compared to the DuraSeal product?**
 9 A We did not have -- that I recall, we
 10 did not compare the two of them in our discussion.
 11 **Q Did he mention anything about the**
 12 **DuraSeal product in the discussion?**
 13 A Not that I remember.
 14 **Q And what were the other benefits of the**
 15 **Adherus product that Dr. Broaddus mentioned?**
 16 MR. ALTHERR: Object to the form.
 17 THE WITNESS: Yeah, I don't recall
 18 others.
 19 BY MR. HUGHES:
 20 **Q Did Dr. Broaddus mention the applicator**
 21 **of the Adherus product?**
 22 A Not that I recall.

Page 168

1 **Q So is it fair to say that the**
 2 **summary -- summary of your discussions with**
 3 **Dr. Broaddus that you relied upon in paragraph 35**
 4 **of your report is that he had used a product in**
 5 **cranial procedures and transsphenoidal procedures**
 6 **and that it -- the Adherus product was easy to**
 7 **use?**
 8 A And that he was favorably impressed --
 9 **Q And favorably --**
 10 A -- correct.
 11 **Q -- impressed.**
 12 A And that he was pleased -- he was
 13 satisfied with it; he was pleased with it.
 14 **Q Did -- did you and Dr. Broaddus discuss**
 15 **the color of the Adherus product?**
 16 A I don't recall if we -- if I
 17 specifically discussed the color with
 18 Dr. Broaddus.
 19 **Q But in forming your opinions in this**
 20 **report, you didn't take into account any**
 21 **discussion of color of [sic] Dr. Broad- --**
 22 **Broaddus; is that accurate?**

Page 169

1 A Correct.
 2 **Q In fact, in forming your opinions in**
 3 **this report on paragraph 35, or anywhere else in**
 4 **your report, did you rely upon your discussions**
 5 **with any other surgeons regarding the color of the**
 6 **Adherus product?**
 7 A I definitely discussed color with the
 8 other surgeons, yes.
 9 **Q These others you mentioned today?**
 10 A Correct.
 11 **Q But that -- those discussions were**
 12 **limited to the difference of Adherus being green**
 13 **versus DuraSeal being blue; correct?**
 14 A I don't -- I can't say with certainty
 15 that was the limitation of the color discussion.
 16 **Q But that's the limitation -- that's --**
 17 **strike that.**
 18 **But that's the limit of the discussion**
 19 **you relied upon in forming your opinions**
 20 **identified in your report?**
 21 MR. ALTHERR: Object to the form.
 22 THE WITNESS: I don't understand the --

<p style="text-align: right;">Page 170</p> <p>1 the difference in what you just asked.</p> <p>2 BY MR. HUGHES:</p> <p>3 Q So you dis- -- you discussed the use of</p> <p>4 the Adherus ET product with various physicians in</p> <p>5 forming your opinions in your report; is that</p> <p>6 accurate?</p> <p>7 A Again I -- I think -- I'm sorry to beat</p> <p>8 this to death. Again you said ET in the product.</p> <p>9 I just want to specify in the conversations I did</p> <p>10 not explicitly say to them the ET product. I said</p> <p>11 the Adherus and the -- or the new dural sealant --</p> <p>12 Q Okay.</p> <p>13 A -- without specifying that it was the</p> <p>14 ET, so --</p> <p>15 Q So in forming your opinions in your</p> <p>16 report, you discussed the Adherus product --</p> <p>17 A Thank you.</p> <p>18 Q -- with other physicians; is that</p> <p>19 accurate?</p> <p>20 A Yes.</p> <p>21 Q And to the degree you discussed colors</p> <p>22 of [sic] those physicians and you relied upon it</p>	<p style="text-align: right;">Page 172</p> <p>1 today.</p> <p>2 BY MR. HUGHES:</p> <p>3 Q And that would have been the same --</p> <p>4 the basis for your opinion when you signed this</p> <p>5 report on August 24th, 2017?</p> <p>6 A Correct.</p> <p>7 Q Just to kind of short circuit a</p> <p>8 example -- remember, you -- you submitted a second</p> <p>9 report in this litigation --</p> <p>10 A Yes.</p> <p>11 Q -- is that accurate?</p> <p>12 And between the time you -- this is</p> <p>13 going to be a yes or no answer, and we can discuss</p> <p>14 more later.</p> <p>15 But between the time of August 24 of</p> <p>16 2017 when you submitted your opening report in</p> <p>17 this litigation and you submitted your second</p> <p>18 report in the litigation, did you have other</p> <p>19 conversations with these individuals that informed</p> <p>20 your opinion in the second report?</p> <p>21 A So I don't recall if any of those</p> <p>22 conversations could have occurred after</p>
<p style="text-align: right;">Page 171</p> <p>1 in your report, that reliance was limited to the</p> <p>2 fact that Adherus is green and DuraSeal is blue;</p> <p>3 is that accurate?</p> <p>4 MR. ALTHERR: Object to the form.</p> <p>5 THE WITNESS: No, I think -- again</p> <p>6 you're -- you're limiting it to just that single</p> <p>7 fact about the color, and it's very possible we</p> <p>8 discussed other elements of the color during those</p> <p>9 conversations.</p> <p>10 BY MR. HUGHES:</p> <p>11 Q I'm not asking what you discussed. I'm</p> <p>12 asking what you relied upon in forming your</p> <p>13 opinions in your report.</p> <p>14 A I stand corrected.</p> <p>15 I relied on all of our conversations in</p> <p>16 forming my opinion.</p> <p>17 Q In forming your opinion, were there any</p> <p>18 other specific facts based on these discussions</p> <p>19 with doctors regarding color other than that</p> <p>20 Adherus is green and DuraSeal is blue?</p> <p>21 MR. ALTHERR: Object to form.</p> <p>22 THE WITNESS: Not that I can recall</p>	<p style="text-align: right;">Page 173</p> <p>1 August 24th --</p> <p>2 Q When we were just discuss- --</p> <p>3 A -- between those two reports.</p> <p>4 Q So we were just discussing the</p> <p>5 individuals that you were implicitly referencing</p> <p>6 in paragraph 35 in the -- the following [verbatim]</p> <p>7 sentence?</p> <p>8 A Yes.</p> <p>9 Q And you don't recall if any of these</p> <p>10 discussions might have occurred after August 24th,</p> <p>11 2017; is that accurate?</p> <p>12 A That's correct. My recollection is</p> <p>13 that after the period -- and I'm estimating</p> <p>14 somewhere around July -- when I was prevented from</p> <p>15 using the device, I don't recall any other -- any</p> <p>16 other conversations I had with anyone in my</p> <p>17 department regarding their impressions of the --</p> <p>18 of the products.</p> <p>19 Q So is it fair to say that any of these</p> <p>20 conversations that you're implicitly referencing</p> <p>21 in paragraph 35 of your report, they did not occur</p> <p>22 after you were not able -- after you requested to</p>

<p style="text-align: right;">Page 174</p> <p>1 use the ET product?</p> <p>2 Strike that. I'll rephrase it.</p> <p>3 Is it fair to say that any of the</p> <p>4 conversations you are referencing in paragraph 35</p> <p>5 of your opening report, that those conversations</p> <p>6 did not occur after the time you requested to use</p> <p>7 the ET product?</p> <p>8 MR. ALTHERR: Object to the form.</p> <p>9 THE WITNESS: I don't think it's fair</p> <p>10 because I can't recall the exact date that I</p> <p>11 requested.</p> <p>12 BY MR. HUGHES:</p> <p>13 Q Is it fair to say that all of these</p> <p>14 conversations that you're referencing in</p> <p>15 paragraph 35 of your -- of your report occurred</p> <p>16 before August 24th, 2017?</p> <p>17 A I believe that to be the case, yes.</p> <p>18 Q Because you reference it in your report</p> <p>19 and you signed the report in August --</p> <p>20 A Correct.</p> <p>21 Q Did you have any follow-up</p> <p>22 conversations with those individuals after you</p>	<p style="text-align: right;">Page 176</p> <p>1 upon those other elements regarding the color</p> <p>2 other -- strike that.</p> <p>3 Did you rely upon those discussions of</p> <p>4 other elements of color when you formed your</p> <p>5 opinion stated in your opening report?</p> <p>6 A Yes, any conversation we had regarding</p> <p>7 color, whether it was simply the difference</p> <p>8 between green and blue or more in-depth</p> <p>9 discussions of the color, I would certainly have</p> <p>10 relied on in forming my opinion --</p> <p>11 Q And --</p> <p>12 A -- (unintelligible) --</p> <p>13 Q -- can you identify any other</p> <p>14 discussions regarding color other than the</p> <p>15 difference between Adherus being green and that</p> <p>16 DuraSeal being blue that you did rely upon in</p> <p>17 forming your opinion?</p> <p>18 A No, not at this time.</p> <p>19 Q Let's keep in tune of paragraph 35 of</p> <p>20 your report -- your opening report.</p> <p>21 A Did you -- what did you say? Keep in</p> <p>22 what?</p>
<p style="text-align: right;">Page 175</p> <p>1 signed this report regarding their use of the ET</p> <p>2 product?</p> <p>3 A Not that I can recall.</p> <p>4 Q And you haven't relied upon any</p> <p>5 conversations with these individuals after</p> <p>6 August 2000 -- after August 24th, 2017, in forming</p> <p>7 your opinions in this litigation?</p> <p>8 A Correct.</p> <p>9 Q Going back just to make sure we --</p> <p>10 we've covered this, paragraph 35 of the opening</p> <p>11 report, the individuals at VCU you mentioned, are</p> <p>12 you relying upon any discussions with them</p> <p>13 regarding color of the Adherus product other than</p> <p>14 the difference that Adherus is green and DuraSeal</p> <p>15 is blue?</p> <p>16 MR. ALTHERR: Object to the form.</p> <p>17 THE WITNESS: Yes, I certainly think</p> <p>18 it's possible we discussed other elements of the</p> <p>19 color.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q Are you relying upon those discussions</p> <p>22 of other elements of the color in -- did you rely</p>	<p style="text-align: right;">Page 177</p> <p>1 Q In tune.</p> <p>2 A Oh.</p> <p>3 Q Keep on the same page?</p> <p>4 A Okay. Yeah.</p> <p>5 Q So at the beginning of paragraph 35,</p> <p>6 you say you also reviewed two videos, and you list</p> <p>7 two names of videos.</p> <p>8 Do you see that?</p> <p>9 A Yes.</p> <p>10 Q Are those the only two videos that you</p> <p>11 reviewed in preparation and you relied upon in</p> <p>12 forming your opinions in this report?</p> <p>13 A No, I think there were other videos.</p> <p>14 Q What videos were those?</p> <p>15 A (Witness reviews document.)</p> <p>16 So -- would you repeat your last</p> <p>17 question?</p> <p>18 Q Yeah. I'll rephrase it again.</p> <p>19 In paragraph 35, in the first sentence</p> <p>20 you identified two videos that you reviewed and</p> <p>21 relied upon for the opinions in -- in -- opinions</p> <p>22 in this report: The Adherus AutoSpray Following</p>

<p style="text-align: right;">Page 178</p> <p>1 Temporal Lobotomy [sic], and the second video is 2 titled Adherus AutoSpray Preparation. 3 Do you see that? 4 A Yes, I do. 5 Q Are these the only two videos that you 6 relied upon in forming your opinions in your 7 opening expert report? 8 A Yes, I believe for this report those 9 are the only two videos I relied on. If I said no 10 earlier, it's because I had some uncertainty as to 11 the time when I viewed other videos, and I -- 12 Q Yeah. 13 A -- don't think for the purposes of this 14 report I reviewed other videos. 15 Q There might be other videos in your 16 second -- 17 A Correct. 18 Q -- report? 19 A That's right. 20 Q And after the "furthermore" sentence in 21 paragraph 35, you say, The appropriate thickness 22 of the coating specified in the Adherus product</p>	<p style="text-align: right;">Page 180</p> <p>1 respective IFUs provided with the HyperBranch 2 products, and my observation of films and actual 3 procedures using those products. 4 What films are you referencing here? 5 A The two videos, Adherus AutoSpray 6 Following Temporal Lobectomy and Adherus AutoSpray 7 Preparation. 8 Q And you're not referring to any other 9 films other than the two videos identified in 10 paragraph 35? 11 A Correct. 12 Q And next you say, "observation," and 13 then "of films and actual procedures." 14 What actual procedures are you 15 referring to here? 16 A The temporal lobectomy was an actual 17 procedure. 18 Q And you're referring to the video 19 titled Adherus AutoSpray Following Temporal 20 Lobectomy? 21 A Yes. I think I've used films 22 interchangeably with video in this case.</p>
<p style="text-align: right;">Page 179</p> <p>1 IFUs is 1 to 2 millimeters. 2 Do you see that? 3 A Yes. 4 Q Is that what you would determine as the 5 predeter- -- predetermined thickness? 6 MR. ALTHERR: Object to the form. 7 THE WITNESS: Not nece- -- I would not 8 necessarily -- a user wouldn't necessarily 9 restrict it to 1 to 2 millimeters. 10 BY MR. HUGHES: 11 Q Okay. And further on down you say, My 12 own observations and the HyperBranch videos 13 demonstrates that the user understands when to 14 stop applying the Adherus product. 15 Do you see that? 16 A Yes. 17 Q And these videos is the only videos 18 earlier -- those are the only two videos you're 19 referring to? 20 A Correct. 21 Q Turn to paragraph 37 of your report. 22 Here you say based on your review of the</p>	<p style="text-align: right;">Page 181</p> <p>1 Q And you say, "actual procedures." So 2 the -- the only actual procedure using the Adherus 3 product that you've observed is the film 4 identified on page 35; is that accurate? 5 A Thirty -- page 35, did you say? 6 Q Paragraph 35. 7 A Are you referring -- yes, if you're 8 referring to the sentence that reads, My own 9 observations and the HyperBranch videos, yes. 10 Q So -- 11 A I -- I -- 12 Q -- have you physically been in the 13 operating procedure [verbatim] to observe a 14 procedure using an Adherus product? 15 A No, I have not. 16 Q Dr. Rivet, do you know who Dr. John 17 Collins is? 18 A Yes. 19 Q Who is Dr. John Collins? 20 A Dr. Collins is a -- if it's who you're 21 speaking of, it's a pediatric neurosurgeon in my 22 department, one of my colleagues.</p>

<p style="text-align: right;">Page 182</p> <p>1 Q And did you discuss the use of the</p> <p>2 Adherus ET product with Dr. Collins?</p> <p>3 A It's possible, but I don't recall it.</p> <p>4 If I can just clarify that. For</p> <p>5 example, he certainly may have been present in</p> <p>6 the -- the discussion I mentioned earlier when</p> <p>7 Dr. Broaddus mentioned it, and he may have made --</p> <p>8 he certainly could have been part of that</p> <p>9 discussion, for example. I don't remember if he</p> <p>10 was present.</p> <p>11 Q And is Dr. Collins a good surgeon?</p> <p>12 A Can you explain what you mean by "a</p> <p>13 good surgeon"?</p> <p>14 Q Do you think Dr. Collins is an adequate</p> <p>15 physician?</p> <p>16 A Yes.</p> <p>17 Q Do you think Dr. Collins is an</p> <p>18 excellent physician?</p> <p>19 A Yes.</p> <p>20 Q Do you think Dr. Collins is an</p> <p>21 excellent surgeon?</p> <p>22 A I don't have too much basis to judge.</p>	<p style="text-align: right;">Page 184</p> <p>1 A I'm not aware of that statement.</p> <p>2 Q Does it surprise you that Dr. Collins</p> <p>3 would say that about DuraSeal?</p> <p>4 A No.</p> <p>5 I'm sorry. Did you say about DuraSeal?</p> <p>6 Q Pardon me. Does it surprise you that</p> <p>7 Dr. Collins would say that about Adherus?</p> <p>8 A No, it doesn't surprise me.</p> <p>9 Q In your use of DuraSeal, have you had</p> <p>10 DuraSeal clump on you?</p> <p>11 A Sure.</p> <p>12 Q Have you had -- in your use of</p> <p>13 DuraSeal, have you started an application of</p> <p>14 DuraSeal and then stopped and reapplied</p> <p>15 application of DuraSeal?</p> <p>16 A Yes.</p> <p>17 Q Did you have to exchange a tip when you</p> <p>18 did that?</p> <p>19 A Yes.</p> <p>20 Q In your opinion, is the ability to</p> <p>21 start and stop without needing to exchange a tip a</p> <p>22 benefit of a dural sealant?</p>
<p style="text-align: right;">Page 183</p> <p>1 I've operated with him several times. He's board</p> <p>2 certified in pediatric neurosurgery. He's more</p> <p>3 experienced than I am and has operated at multiple</p> <p>4 institutions. He's integrated advanced</p> <p>5 technologies. So I have a very favorable</p> <p>6 impression.</p> <p>7 Q Do you respect Dr. Collins' opinions</p> <p>8 regarding neurosurgery?</p> <p>9 A Yes.</p> <p>10 Q Do you respect Dr. Collins' opinions</p> <p>11 regarding devices used in neurosurgery?</p> <p>12 A I respect his opinions.</p> <p>13 Q And are you aware that Dr. Collins has</p> <p>14 used the Adherus device?</p> <p>15 A No. As I said, if we discussed it, I</p> <p>16 don't recall it.</p> <p>17 Q And are you aware that Dr. Collins has</p> <p>18 stated that the Adherus device is an improvement</p> <p>19 over DuraSeal?</p> <p>20 A I'm not aware of that.</p> <p>21 Q And that, you know, it doesn't clump</p> <p>22 and harden too quickly?</p>	<p style="text-align: right;">Page 185</p> <p>1 A Yes.</p> <p>2 Q Are you aware that Dr. Collins has</p> <p>3 suggested that the Adherus product should be used</p> <p>4 as an alternative to the DuraSeal because of its</p> <p>5 improved features?</p> <p>6 MR. ALTHERR: Object to the form.</p> <p>7 THE WITNESS: I'm not aware of that</p> <p>8 statement.</p> <p>9 BY MR. HUGHES:</p> <p>10 Q Does it surprise you that Dr. Collins</p> <p>11 would say that about the Adherus product?</p> <p>12 A No.</p> <p>13 Q Based on your discussions with the</p> <p>14 individuals we were referring to earlier at VCU</p> <p>15 and their use, would it surprise you if they</p> <p>16 thought use of the Adherus product would be a</p> <p>17 benefit for VCU over the use of DuraSeal?</p> <p>18 MR. ALTHERR: Object to the form.</p> <p>19 THE WITNESS: No, it would not surprise</p> <p>20 me.</p> <p>21 BY MR. HUGHES:</p> <p>22 Q Dr. Rivet, are you aware that other</p>

<p style="text-align: right;">Page 186</p> <p>1 doctors and other surgeons have testified in this</p> <p>2 litigation?</p> <p>3 A Yes.</p> <p>4 Q And are you aware that approximately</p> <p>5 nine surgeons have testified in this litigation?</p> <p>6 A Yes.</p> <p>7 Q Did you consider the testimony of any</p> <p>8 of those nine surgeons when forming your opinion</p> <p>9 stated in your expert report dated August 24th,</p> <p>10 2017?</p> <p>11 A No.</p> <p>12 Q Why did you choose not to evaluate the</p> <p>13 testimony of the nine other surgeons who testified</p> <p>14 in this litigation when forming your opinion in</p> <p>15 your opening report?</p> <p>16 MR. ALTHERR: Object to the form.</p> <p>17 THE WITNESS: I don't think I was aware</p> <p>18 of the testimony and certainly would and have</p> <p>19 reviewed it.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q So when you signed your opening report</p> <p>22 on August 24th, 2017 --</p>	<p style="text-align: right;">Page 188</p> <p>1 aware of other surgeon testimony in this</p> <p>2 litigation, you would have wanted to review that?</p> <p>3 A Yes.</p> <p>4 Q And as of August 24th, 2017, you were</p> <p>5 not aware of any other surgeon testimony in this</p> <p>6 litigation?</p> <p>7 A I believe that's correct.</p> <p>8 Q And you did not rely upon any other</p> <p>9 surgeon testimony in this litigation when forming</p> <p>10 the opinions stated in your August 24th, 2017</p> <p>11 test- -- report; is that accurate?</p> <p>12 A Would you rephrase that, please?</p> <p>13 Q Yeah.</p> <p>14 You did not rely upon any other surgeon</p> <p>15 testimony given in this litigation when forming</p> <p>16 the opinions stated in your August 24th, 2017</p> <p>17 report?</p> <p>18 MR. ALTHERR: Object to the form.</p> <p>19 THE WITNESS: Correct.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q Before we just started talking about</p> <p>22 this today, are you aware that nine -- are you</p>
<p style="text-align: right;">Page 187</p> <p>1 A Yes.</p> <p>2 Q -- you were not aware of the other</p> <p>3 doctor testimony in this litigation?</p> <p>4 A I don't recall if I was aware because I</p> <p>5 would normally -- I would be interested -- very</p> <p>6 interested in, as I was at VCU, any other</p> <p>7 surgeon's impressions of a product in forming an</p> <p>8 opinion.</p> <p>9 Q So on August 24th, 2017, and before, if</p> <p>10 you were aware of other surgeon deposition</p> <p>11 testimony in this litigation, you would have</p> <p>12 wanted to review that test- -- that testimony?</p> <p>13 A Yes.</p> <p>14 Q But you did not review any other doctor</p> <p>15 testimony prior to August 24th, 2017 --</p> <p>16 A That is --</p> <p>17 Q -- in this litigation?</p> <p>18 A I think Dr. Mays is a doctor. If you</p> <p>19 mean other surgeons, I don't recall reviewing</p> <p>20 other surgeons' testimony.</p> <p>21 Q Yeah, I'll strike that to be clear.</p> <p>22 So as of August 24th, 2017, if you were</p>	<p style="text-align: right;">Page 189</p> <p>1 aware that other surgeons gave testimony in this</p> <p>2 litigation?</p> <p>3 A Yes.</p> <p>4 Q When did you become aware of that?</p> <p>5 A When I read the rebuttal report that</p> <p>6 indicated I had not reviewed it.</p> <p>7 Q And you submitted a rebuttal report in</p> <p>8 this litigation; correct?</p> <p>9 A That's correct.</p> <p>10 Q The rebuttal report you submitted would</p> <p>11 have been submitted in the same day as the</p> <p>12 rebuttal report you were just mentioning; is that</p> <p>13 accurate?</p> <p>14 A I don't know the answer to that.</p> <p>15 Q Did you submit your rebuttal report in</p> <p>16 this litigation prior to reviewing the report you</p> <p>17 just mentioned regarding the doc- -- the surgeon</p> <p>18 testimony?</p> <p>19 A I don't -- I'd have to check the dates.</p> <p>20 I don't know the answer to that.</p> <p>21 Q We can come back to this a little bit</p> <p>22 later on.</p>

<p style="text-align: right;">Page 190</p> <p>1 A Sure.</p> <p>2 Q Before today, have you reviewed surgeon</p> <p>3 testimony given in this litigation?</p> <p>4 A Yes.</p> <p>5 Q When did you review that surgeon</p> <p>6 testimony?</p> <p>7 A Over the last -- in the last month,</p> <p>8 approximately.</p> <p>9 Q Was this after you submitted your</p> <p>10 rebuttal report in this litigation?</p> <p>11 A I believe it was, yes.</p> <p>12 Q Okay. Was it --</p> <p>13 A Again, I -- I think you're reasking the</p> <p>14 same question. I said it would be nice to look at</p> <p>15 the dates on --</p> <p>16 Q Yeah.</p> <p>17 A -- those reports, but . . .</p> <p>18 Q I'm not trying to play a game. We'll</p> <p>19 get there in a second.</p> <p>20 A Okay.</p> <p>21 Q Was that review of the surgeon</p> <p>22 testi- -- did you review the surgeon testimony in</p>	<p style="text-align: right;">Page 192</p> <p>1 MR. ALTHERR: Object to form.</p> <p>2 THE WITNESS: No, I would expect a</p> <p>3 statement like that for components of some of</p> <p>4 these patents.</p> <p>5 BY MR. HUGHES:</p> <p>6 Q Are you a person of ordinary skill in</p> <p>7 this case?</p> <p>8 A I guess it depends on the definition.</p> <p>9 I -- I have a bachelor of science in chemistry. I</p> <p>10 think it's one of the things you read. And my --</p> <p>11 my skill -- my -- my role in this is as a</p> <p>12 neurosurgeon. So I'm not a polymer chemist which</p> <p>13 I think Dr. Mays is.</p> <p>14 Q When you signed your opening report on</p> <p>15 August 24th, 2017, did you consider yourself a</p> <p>16 person of ordinary skill in this litigation?</p> <p>17 A Can you define that? Are you defining</p> <p>18 it as you read the paragraph?</p> <p>19 Q Well, I'm saying in your mind, had you</p> <p>20 considered your level of skill in comparison to</p> <p>21 the level of ordinary skill in the art -- a person</p> <p>22 of ordinary skill in the art when you submitted</p>
<p style="text-align: right;">Page 191</p> <p>1 this litigation in preparation for your deposition</p> <p>2 today?</p> <p>3 A Yes.</p> <p>4 Q Are you familiar with the term "person</p> <p>5 of ordinary skill" in patent law?</p> <p>6 A Yes.</p> <p>7 Q And are you aware of what the level of</p> <p>8 skill is of the person of ordinary skill as</p> <p>9 identified in this litigation?</p> <p>10 MR. ALTHERR: Object to the form.</p> <p>11 THE WITNESS: No.</p> <p>12 BY MR. HUGHES:</p> <p>13 Q If I represented that Dr. Mays had said</p> <p>14 that a person of ordinary skill contains a Ph.D.</p> <p>15 degree or equivalent education in polymer</p> <p>16 chemistry or someone having a bachelor of science</p> <p>17 degree in chemistry or closely related field and</p> <p>18 several years of experience in the development and</p> <p>19 manufacture of polymer materials for use as tissue</p> <p>20 sealants, would that surprise you that that's</p> <p>21 Dr. Mays' opinion regarding the level of ordinary</p> <p>22 skill?</p>	<p style="text-align: right;">Page 193</p> <p>1 your opening report?</p> <p>2 A Yes.</p> <p>3 MR. ALTHERR: Object to the form.</p> <p>4 THE WITNESS: Yes.</p> <p>5 BY MR. HUGHES:</p> <p>6 Q At that time you had considered it?</p> <p>7 A Yes.</p> <p>8 Q And what was your opinion at that</p> <p>9 time -- where is your opinion regarding your level</p> <p>10 of skill regarding a person of ordinary skill in</p> <p>11 the art found in your opening report?</p> <p>12 A I don't understand your question.</p> <p>13 Q Let's take -- go at this a slightly</p> <p>14 different way. Go to page 19 -- paragraph 19 of</p> <p>15 your report.</p> <p>16 A Paragraph 19.</p> <p>17 Q Uh-huh.</p> <p>18 And you say I am using the definition</p> <p>19 of the terms as I understand them as a</p> <p>20 neurosurgeon.</p> <p>21 A Exactly.</p> <p>22 Q Do you see that?</p>

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1 And do you believe you are qualified as
 2 an expert witness regards to neurosurgery?
 3 A Yes.
 4 Q And look at paragraph 9 of your report.
 5 One moment. Pardon me.
 6 Look at paragraph 12 in your report.
 7 And you say I am qualified to testify in how an
 8 ordinary skilled neurosurgeons or spinal surgeon
 9 understand their use of various products [as
 10 read].
 11 Do you see that?
 12 A Yes, I do.
 13 Q Do you identify in your report --
 14 anywhere else where you identify yourself as a
 15 person of ordinary skill in relation to the
 16 patents in this investigation?
 17 MR. ALTHERR: Object to the form.
 18 THE WITNESS: Yeah, I don't understand
 19 your question.
 20 BY MR. HUGHES:
 21 Q Look at paragraph 19, please, of your
 22 report on page 9.

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1 A I have paragraph 19 on page 7 on mine.
 2 Q Yeah, but I -- 19 -- paragraph 19 lasts
 3 for a few pages. Look at specifically page 9.
 4 A Understood. Thank you.
 5 Q And just below the two bullet points --
 6 A Uh-huh.
 7 Q -- you'll see a sentence that begins, I
 8 am not a chemist, biochemist or designer of
 9 polymers.
 10 Do you see that?
 11 A Yes, I do.
 12 Q Do you have -- you said you have a
 13 bachelor's of science in chemistry; correct?
 14 A Correct.
 15 Q But here you say you're not a chemist;
 16 is that accurate?
 17 A That is accurate.
 18 Q Do you consider yourself an expert in
 19 chemistry?
 20 A I do --
 21 MR. ALTHERR: Object --
 22 THE WITNESS: -- not.

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1 MR. HUGHES: -- to form.
 2 BY MR. HUGHES:
 3 Q Do you consider yourself an expert in
 4 biochemistry?
 5 A I do not.
 6 Q Do you consider yourself an expert in
 7 the design of polymers?
 8 A I do not.
 9 Q Do you consider yourself an expert in
 10 hydrogels?
 11 A I guess it defines on -- depends on
 12 the -- the --
 13 Q I'll rephrase.
 14 A Yeah.
 15 Q Do you define yourself as an expert in
 16 the formulation and making of hydrogels?
 17 A I do not.
 18 Q Do you consider yourself an expert in
 19 the formulation or making of polymers?
 20 A I do not.
 21 Q Do you consider yourself an expert in
 22 pathology?

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1 A What do you mean by "pathology"?
 2 Q The field of -- medical field of
 3 pathology.
 4 A No.
 5 Q And do you consider yourself an expert
 6 in histological techniques?
 7 A No.
 8 Q Have you ever studied the formulation
 9 of hydrogels?
 10 A Can you define "studied"?
 11 Q Have you ever investigated academically
 12 or professionally the formulation and
 13 manufacturing of hydrogels?
 14 A Yes.
 15 Q Is that -- is that identified in your
 16 report?
 17 A No.
 18 Q Okay. But you testified you don't
 19 consider yourself an expert in hydrogels?
 20 A Correct.
 21 Q Okay.
 22 A And you said you specified the

<p style="text-align: right;">Page 198</p> <p>1 manufacturer and other -- you clarified -- when I</p> <p>2 said hydrogels, you clarified further. That's</p> <p>3 what I said no to.</p> <p>4 Q Okay.</p> <p>5 A But I will not -- I'm clarifying that</p> <p>6 because this case involves the use of hydrogels in</p> <p>7 spinal surgery, so if we're going to expand the</p> <p>8 question of hydrogels to include their use in</p> <p>9 spinal surgery and cranial surgery, the answer is</p> <p>10 no.</p> <p>11 But I think you -- you specified</p> <p>12 further, and that's what I mean by -- when I say</p> <p>13 no.</p> <p>14 Q And for the bases of the report -- your</p> <p>15 opening report, you're opining on your bases as an</p> <p>16 expert as a neurosurgeon?</p> <p>17 A Correct. I would add spinal surgeon</p> <p>18 just to -- just to -- clear that we're not</p> <p>19 excluding an orthopedic spine surgeon or</p> <p>20 something.</p> <p>21 Q Understood. Understood.</p> <p>22 A Okay. Thank you.</p>	<p style="text-align: right;">Page 200</p> <p>1 Q And in those discussions with Dr. Mays,</p> <p>2 did you ever discuss the level of ordinary skill</p> <p>3 on how you may or may not be one of ordinary skill</p> <p>4 in the art?</p> <p>5 MR. ALTHERR: Object to the form.</p> <p>6 THE WITNESS: He -- he -- I think the</p> <p>7 reason for our discussion -- we -- we did</p> <p>8 discuss -- that is that some of the things</p> <p>9 you're -- the biochemistry, the polymer chem- --</p> <p>10 chemistry, I --</p> <p>11 BY MR. HUGHES:</p> <p>12 Q We can get that a little bit later on.</p> <p>13 But for POSA, a person of ordinary skill in the</p> <p>14 art --</p> <p>15 A Yeah.</p> <p>16 Q -- specifically.</p> <p>17 A And I'm --</p> <p>18 MR. ALTHERR: Counsel, I'm going to</p> <p>19 object to you talking over the witness before he's</p> <p>20 had a chance to finish his answer. Please let him</p> <p>21 finish his answer before you start talking over</p> <p>22 him.</p>
<p style="text-align: right;">Page 199</p> <p>1 Q And you're not attempting to opine on</p> <p>2 the technical features of the asserted patents in</p> <p>3 this case?</p> <p>4 MR. ALTHERR: Object to the form.</p> <p>5 THE WITNESS: Right. I don't agree</p> <p>6 with that statement. I think the use of it during</p> <p>7 surgery is a technical feature.</p> <p>8 BY MR. HUGHES:</p> <p>9 Q Okay.</p> <p>10 A It could be construed as a technical</p> <p>11 feature, I should say, and in my opinion in some</p> <p>12 ways is.</p> <p>13 Q Okay. Well, we can get back to that.</p> <p>14 Did you ever discuss the level of</p> <p>15 ordinary skill in regards to the patents with</p> <p>16 Dr. Mays?</p> <p>17 A I'm not sure I understand what you're</p> <p>18 asking.</p> <p>19 Q You -- you -- in your report you</p> <p>20 identify that you spoke with Dr. Mays about</p> <p>21 various things?</p> <p>22 A Yes.</p>	<p style="text-align: right;">Page 201</p> <p>1 MR. HUGHES: Pardon me, Counsel. I</p> <p>2 thought he was finished with his answer.</p> <p>3 THE WITNESS: It's possible we</p> <p>4 discussed POSA without explicitly using that term.</p> <p>5 I don't have enough of an understanding to know</p> <p>6 what would define a discussion of POSA between</p> <p>7 Dr. Mays and myself.</p> <p>8 BY MR. HUGHES:</p> <p>9 Q Okay. Looking at Exhibit 1 to your</p> <p>10 report -- your opening report, what is Exhibit 1?</p> <p>11 A I have Exhibit 1 is -- is my -- my CV,</p> <p>12 my curriculum vitae.</p> <p>13 Q And is this a full and accurate</p> <p>14 curriculum vitae as of August 24th, 2017?</p> <p>15 A I believe it is.</p> <p>16 Q And when you were preparing this report</p> <p>17 that you submitted on August 24th, 2017, how much</p> <p>18 time did you spend preparing it?</p> <p>19 A The entire report?</p> <p>20 Q Let me put it this way. Before you</p> <p>21 submitted this report -- and I -- well, including</p> <p>22 August 27, 2017 [verbatim], how much time had you</p>

<p style="text-align: right;">Page 202</p> <p>1 spent on this litigation from the time you were</p> <p>2 first engaged to writing this report?</p> <p>3 A I don't know the answer to that</p> <p>4 question.</p> <p>5 Q Have you submitted any invoices for</p> <p>6 your time in this litigation thus far?</p> <p>7 A No, I haven't.</p> <p>8 Q Approx- -- when you were writing this</p> <p>9 report itself, the one that went in August 24th,</p> <p>10 2017, approximately how much time did you spend</p> <p>11 writing the report?</p> <p>12 A So the report is -- you know, it was</p> <p>13 not done in one sitting and certainly it was an</p> <p>14 iterative process, and I would estimate --</p> <p>15 Are you including the review of the</p> <p>16 materials in preparation of that report or the</p> <p>17 actual writing?</p> <p>18 Q Well, let's handle both. The actual</p> <p>19 writing, how long did you spend actually writing</p> <p>20 the report?</p> <p>21 A I would say hours. Between four and</p> <p>22 eight hours.</p>	<p style="text-align: right;">Page 204</p> <p>1 A You just rephrased the question in</p> <p>2 another way.</p> <p>3 Q Okay.</p> <p>4 A I said it -- it's -- it -- it could be</p> <p>5 over 20 hours.</p> <p>6 Q Okay.</p> <p>7 A Twenty hours is an estimate which means</p> <p>8 the time period could be above or below 20 hours.</p> <p>9 I'm trying to approximate.</p> <p>10 Q But it's fair to say approximately 20</p> <p>11 hours?</p> <p>12 A Yes, that's fair.</p> <p>13 Q Looking at paragraph 12 of your report,</p> <p>14 Dr. Rivet, you state --</p> <p>15 A I'm there. Thank you.</p> <p>16 Q -- you state -- I believe it's the</p> <p>17 second sentence -- My education, skill and</p> <p>18 experience also qualify me to testify on how an</p> <p>19 ordinary skilled neurosurgeon or spinal surgeon</p> <p>20 would understand the benefits of using</p> <p>21 FDA-approved products for their approved uses as</p> <p>22 compared to using off-label products.</p>
<p style="text-align: right;">Page 203</p> <p>1 Q Between four and eight hours writing</p> <p>2 the report.</p> <p>3 And what about the review of materials</p> <p>4 related to your report? How long did you spend on</p> <p>5 that?</p> <p>6 A Also hours. For example, the patents</p> <p>7 are -- some of them are lengthy, and I read them.</p> <p>8 Q Would it be more than ten hours?</p> <p>9 A No, I think ten hours is a -- is a</p> <p>10 reasonable approximation of the time spent</p> <p>11 reviewing materials to prepare the report.</p> <p>12 Q So in combined of writing the report</p> <p>13 and reviewing materials for the report, it would</p> <p>14 be on the order of 18 or 20 hours; is that fair to</p> <p>15 say?</p> <p>16 A Yes, sir, I think that's fair.</p> <p>17 Q But it wouldn't be more than 20 hours?</p> <p>18 A It could have been.</p> <p>19 Q But it's fair to say it was 20 hours or</p> <p>20 less?</p> <p>21 A No.</p> <p>22 Q Okay.</p>	<p style="text-align: right;">Page 205</p> <p>1 And it continues with a parenthetical</p> <p>2 on the next page.</p> <p>3 Do you see that?</p> <p>4 A Yes, I do.</p> <p>5 Q Where in your report that was submitted</p> <p>6 on October 24th, 2017, are these opinions</p> <p>7 expressed?</p> <p>8 A Define "these opinions."</p> <p>9 Q The opinions referring to your</p> <p>10 experience allows you to testify how an ordinary</p> <p>11 skilled neurosurgeon and spinal surgeon would</p> <p>12 understand the benefits of using FDA approved, as</p> <p>13 the sentence goes on.</p> <p>14 So you're expressing an opinion in that</p> <p>15 sentence; is that accurate?</p> <p>16 A Yes, I think that sentence is an</p> <p>17 opinion.</p> <p>18 Q And regarding the use of FDA-approved</p> <p>19 products for their approved uses comparing --</p> <p>20 compared to off-label products, where in your</p> <p>21 report are your opinions regarding using</p> <p>22 FDA-approved products for their approved uses as</p>

<p style="text-align: right;">Page 206</p> <p>1 compared to using off-label products -- where are 2 those opinions stated in this report? 3 A I don't think there's other discussion 4 of off-label or on-label device use other than 5 this sentence in paragraph 12 that you stated. 6 Q So there's no other identification in 7 your report of on-label versus off-label use other 8 than the sentence in paragraph 12? 9 A Within the limitation of I have not 10 gone through during this deposition and reviewed 11 every single paragraph, yes, I believe that to be 12 the case. 13 Q Well, if you'd like to take a short 14 while, your report -- 15 A I believe that to be the case. 16 Q Okay. 17 A I mean -- 18 Q But you don't have any identification 19 of anywhere else in your report that you identify 20 the benefits of using FDA-approved products for 21 their approved uses as compared to using off-label 22 products?</p>	<p style="text-align: right;">Page 208</p> <p>1 A I -- 2 Q What -- 3 A -- think -- 4 Q -- did -- 5 A -- that's -- 6 Q -- you -- 7 A -- that -- 8 Q Let me -- 9 A -- could be -- 10 Q -- restate this. What did you mean by 11 your purchasing? 12 A Sure. Yeah. Thank you. 13 So I was a head of a neurosurgery 14 department for seven years. I've had -- I've been 15 the head in multiple hospitals. As in that role, 16 we make decisions regarding what purchases should 17 be made for the operating room, et cetera. I've 18 advised the operating room on purchases at my 19 current position, but I personally with my own 20 money never purchased products from either the 21 plaintiffs or defendant. Just -- 22 Q So your purchasing would have been in</p>
<p style="text-align: right;">Page 207</p> <p>1 A That's correct. I don't know of any 2 other locations that I have any comment regarding 3 off- or on-label device. 4 Q And did you have any -- did you express 5 any other opinions regarding that in this report? 6 A Other than the sentence you point out, 7 I don't think I did. That's correct. 8 Q Look at paragraph 14. 9 A Okay. 10 Q It states, Aside from former positions 11 where I commercially purchased (or tested products 12 for potential commercial purchase) from either the 13 plaintiffs or defendant, I have not had a prior 14 professional relationship with any of the parties 15 in this matter. 16 Have you previously purchased DuraSeal 17 product? 18 A Can we define what my purchasing -- can 19 we define that a little bit -- 20 Q What -- 21 A -- better? 22 Q What --</p>	<p style="text-align: right;">Page 209</p> <p>1 your professional capacity for either your use as 2 a surgeon or for the use as your department as a 3 surgeon? 4 A That's right. Or for my colleagues' 5 use. That's better phrased, yes. 6 Q And you -- you've never purchased 7 the -- the Adherus or the -- the DuraSeal product 8 for your personal use? 9 A That's correct. 10 Q And you said tested products for 11 potential commercial use [verbatim]. 12 Is that in the context you just 13 mentioned of -- of -- as a purchasing agent of 14 testing products for potential purpose? 15 A That's correct. 16 What I mean by that is sort of what we 17 were discussing earlier, the process by which we, 18 as surgeons, test -- and I put that in quotes -- 19 evaluate an FDA-approved product for the decision 20 about whether to integrate it into our practice or 21 the department's practice. And I've done that in 22 multiple contexts in multiple hospitals.</p>

<p style="text-align: right;">Page 210</p> <p>1 Q Is your testimony here limited to 2 FDA-approved products, the testimony in 3 paragraph 14? 4 A No, it is not. I have evaluated 5 products as part of clinical trials for non-FDA 6 approved. 7 Q Have you ever evaluated products from 8 either the plaintiffs or the defendant in 9 non-FDA -- or clinical trials prior to FDA use? 10 A No. 11 I believe you asked that earlier in the 12 day, and I -- my answer is not that I'm aware. 13 But I -- 14 Q Oh. 15 A -- did not participate in any trials 16 for either of the -- 17 Q I'm just -- 18 A -- products -- 19 Q -- trying to ask in context of 20 paragraph 14 to make sure I understand the scope 21 of what you're referring to in paragraph 14 here. 22 So prior to this litigation, have you</p>	<p style="text-align: right;">Page 212</p> <p>1 at it could -- there may have been an 2 investigation going on. As a resident, there may 3 have been a time where there was a study I was 4 involved with and just frankly not been aware of 5 it, so -- but within the limits of that, no. 6 Q Understood. 7 And the plaintiffs you're referring to, 8 the Integra LifeSciences Corporation, Integra 9 LifeSciences Sales, Confluent Surgical and Incept 10 LLC? 11 A Inclusive of all of those, yes. 12 Q And is that -- also, the statement's 13 inclusive of any other Integra entity? 14 A Yes. 15 Q Have you ever attended any retreats or 16 conferences sponsored by Integra where your 17 travel, lodging or entertainment was paid for? 18 A No, not that I'm aware of. 19 Q The same question for Confluent 20 Surgical? 21 A No, not that I'm aware of. 22 Q And for Incept LLC?</p>
<p style="text-align: right;">Page 211</p> <p>1 ever received money or -- yeah, prior to this 2 litigation have you ever received money from the 3 plaintiffs -- any of the plaintiffs? 4 MR. ALTHERR: Object to the form. 5 MR. HUGHES: Strike that. 6 BY MR. HUGHES: 7 Q Prior to your engagement in this 8 litigation, have you ever been compensated by any 9 of the plaintiffs in this litigation? 10 A I -- no. 11 Q And you've never worked on a advisory 12 panel of theirs? 13 A That's correct. 14 Q You've never been a -- you've never 15 done any clinical trials for them, the plaintiffs? 16 A None that I know of, that's correct. 17 Certainly none that I was a principal investigator 18 or associate investigator or in some way named as 19 an investigator by either the plaintiffs or the 20 defendants. 21 I think I mentioned this earlier. It's 22 possible at an institution I was -- I was present</p>	<p style="text-align: right;">Page 213</p> <p>1 A Correct, not that I'm aware of. 2 You said travel, lodging or -- 3 Q Entertainment. 4 A Entertainment. 5 Correct. 6 Q Would there be a situation where any of 7 the plaintiffs had paid for -- would there be a 8 situation where you received any, you know, 9 benefits in kind from any of the plaintiffs? 10 MR. ALTHERR: Object to the form. 11 THE WITNESS: No. 12 I'm just going to make a comment to 13 make -- to clarify this. Integra is a sponsor of 14 some of the national meetings for neurosurgeons 15 and spinal surgeons, and I have attended these 16 meetings. And it is true that I believe Integra 17 provided funds to the sponsors of the meeting. 18 In no way did I receive any direct 19 compensation in kind or any other direct benefit 20 from the fact they sponsored the meeting other 21 than the meeting occurred for myself and my 22 colleagues, if that answers the -- if this</p>

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1 addresses the . . .

2 BY MR. HUGHES:

3 **Q Yes. Thank you.**

4 **If you could quickly look at Exhibit 2**

5 **of your expert report. What is Exhibit 2 to your**

6 **expert report?**

7 A Exhibit 2 is In The United States

8 District Court for Delaware, Integra LifeSciences,

9 plaintiffs versus Hyperbranch, CA Number

10 15-819-LPS-CJB, Plaintiffs Integra LifeSciences

11 Corp., Integra LifeSciences Sales, Confluent

12 Surgical and Incept's final infringement

13 contentions.

14 THE WITNESS: I'm sorry if I read

15 initially -- you warned me. I apologize.

16 BY MR. HUGHES:

17 **Q And you relied upon Integra's final**

18 **infringement contentions in forming your opinions**

19 **in this report; correct?**

20 A That's correct.

21 **Q On page 2 --**

22 A Okay.

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1 **Q -- of the final infringement**

2 **contentions, about six lines down the infringement**

3 **contentions state, Plaintiffs further incorporate**

4 **by reference in their entirety the expert report**

5 **of Dr. Jimmy W. Mays submitted in plaintiffs'**

6 **motion for preliminary injunction and the rebuttal**

7 **expert testimony of Dr. Jimmy W. Mays submitted in**

8 **support of plaintiffs' reply in support of motion**

9 **for a preliminary injunction (respectively D.I.**

10 **10-6 and D.I. 122, Exhibit 6).**

11 Do you see that?

12 A I do.

13 **Q Did you review either of these**

14 **documents in -- in preparation of this report?**

15 A Yes, I reviewed portions of those

16 documents.

17 **Q You reviewed portions of the documents?**

18 A That's correct.

19 **Q What portions of the documents did you**

20 **review?**

21 A The portions that were germane to the

22 areas I'm opining about.

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1 **Q Can you identify what portions of the**

2 **reports are germane to the areas you're opine --**

3 **you're opining about?**

4 A I don't have a copy in front of me.

5 **Q Why did you not identify those reports**

6 **in paragraph 15 of your expert report?**

7 MR. ALTHERR: Object to the form.

8 THE WITNESS: (Reviews document.)

9 I believe the reports were reviewed

10 probably contemporaneously, if not simultaneously,

11 on the phone conversations with -- with Dr. Mays,

12 but I agree it is not listed.

13 BY MR. HUGHES:

14 **Q So it's accurate to say that your**

15 **review of those reports were contemporaneous with**

16 **your discussions with Dr. Mays?**

17 A Portions of them, yes.

18 **Q And the portions that you reviewed and**

19 **relied upon in forming your opinions in this**

20 **report, those were reviewed contemporaneously with**

21 **your discussions with Dr. Mays; is that accurate?**

22 A Yes, some of them that's correct.

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1 **Q Some of them. So there were other**

2 **portions that you relied upon you did not review**

3 **in your discussions with Dr. Mays?**

4 A There were portions that I reviewed

5 that were not at the same time as the phone

6 conversation; that in time were done at a

7 different period.

8 **Q Approximately how long did you spend**

9 **reviewing these reports that Dr. Mays identified**

10 **in the infringement contentions?**

11 A The expert report of Dr. Mays submitted

12 in support of plaintiff's motion for preliminary

13 injunction and the rebuttal report?

14 **Q Correct. D.I. 10-6 and D.I. 122**

15 **identified on page 2 of the infringement**

16 **contentions.**

17 A I would estimate -- you know, an hour

18 for each of them, I would estimate, for the

19 portions I reviewed.

20 **Q And you said earlier it was**

21 **approximately eight to ten hours reviewing**

22 **materials in total in preparation --**

<p style="text-align: right;">Page 218</p> <p>1 A Yes --</p> <p>2 Q -- of your --</p> <p>3 A -- and I --</p> <p>4 Q -- report?</p> <p>5 A -- would -- yes, and I would include</p> <p>6 the review of these in that report.</p> <p>7 Q Okay.</p> <p>8 A In that time, I should say, for the</p> <p>9 report.</p> <p>10 Q Are there any other materials that you</p> <p>11 relied upon in forming your opinion in this report</p> <p>12 other than the discussion we were talking about in</p> <p>13 paragraph 35 in the -- the following [verbatim]</p> <p>14 sentence, and other than these -- Dr. Mays'</p> <p>15 reports with -- identified in the infringement</p> <p>16 contentions?</p> <p>17 Are there any other materials that you</p> <p>18 relied upon in forming your opinions that are not</p> <p>19 listed in paragraph 15?</p> <p>20 MR. ALTHERR: Object to the form.</p> <p>21 THE WITNESS: Would you mind repeating</p> <p>22 that question?</p>	<p style="text-align: right;">Page 220</p> <p>1 A I agree.</p> <p>2 Q And the --</p> <p>3 A Correct.</p> <p>4 Q -- two videos you identify in</p> <p>5 paragraph 35, those are not identified in</p> <p>6 paragraph 15, are they?</p> <p>7 A I think they were identified under</p> <p>8 maybe -- under the eighth bullet, I believe,</p> <p>9 they're listed. It reads, The following videos</p> <p>10 that I understand are or --</p> <p>11 Q Oh.</p> <p>12 A -- were once available on HyperBranch's</p> <p>13 Web site.</p> <p>14 Q Thank you.</p> <p>15 Are there any other materials that you</p> <p>16 relied upon in forming your opinions that are not</p> <p>17 listed in paragraph 15?</p> <p>18 A Or in 35 or in the infringements?</p> <p>19 Q Correct. Yeah.</p> <p>20 A If you allow me to summarize, so we</p> <p>21 have the paragraph 15. We have the paragraph 35.</p> <p>22 And as you've pointed out, we have the</p>
<p style="text-align: right;">Page 219</p> <p>1 BY MR. HUGHES:</p> <p>2 Q Are there any other materials that you</p> <p>3 relied upon in forming your opinions in this</p> <p>4 report other than these two Dr. Mays reports in</p> <p>5 the infringement contentions and other than the</p> <p>6 conversations in paragraph 35 that we discussed</p> <p>7 because those aren't identified in paragraph 15,</p> <p>8 are they?</p> <p>9 MR. ALTHERR: Object to the form.</p> <p>10 BY MR. HUGHES:</p> <p>11 Q Here, I'll step back.</p> <p>12 So the two reports for Dr. Mays</p> <p>13 identified in the infringement conte- --</p> <p>14 contentions, those are not listed in paragraph 15,</p> <p>15 are they?</p> <p>16 A I agree.</p> <p>17 Q And the conversations you reference in</p> <p>18 paragraph 35 of your report, those conversations</p> <p>19 are --</p> <p>20 A Ah.</p> <p>21 Q -- not identified in paragraph 15, are</p> <p>22 they?</p>	<p style="text-align: right;">Page 221</p> <p>1 infringement, specifically two reports -- expert</p> <p>2 reports from Dr. Mays. We'll call those three</p> <p>3 things.</p> <p>4 And those -- besides those three, I am</p> <p>5 not aware of other things that are relied on for</p> <p>6 my opinion.</p> <p>7 Q Okay. When did you first become aware</p> <p>8 of HyperBranch Medical Technology as a company?</p> <p>9 A In that period between the fall of</p> <p>10 2016 -- October 2016 through -- through the</p> <p>11 spring. Obviously, at the time of engagement, I</p> <p>12 was aware of the company, both -- so it was</p> <p>13 sometime in there when I found out about this</p> <p>14 product that we were trialing at VCU.</p> <p>15 Q And was that the same time frame you</p> <p>16 were first aware of any product from HyperBranch?</p> <p>17 A Yes, those occurred at the same time.</p> <p>18 Q And are you aware of any other products</p> <p>19 by HyperBranch other than the four accused</p> <p>20 products in this investigation?</p> <p>21 A I do not know any details about their</p> <p>22 other products.</p>

<p style="text-align: right;">Page 222</p> <p>1 Q And you've never purchased an Adherus</p> <p>2 product; correct?</p> <p>3 A If we can go back to the definition of</p> <p>4 purchasing, I, myself, with my own funds, have</p> <p>5 never purchased anything from Adherus. It is</p> <p>6 possible that the department I'm part of, my</p> <p>7 institution, has purchased those Adherus products</p> <p>8 that we're trialing, and I don't know the answer</p> <p>9 to that.</p> <p>10 But my -- I personally have not</p> <p>11 purchased any.</p> <p>12 Q And you've never tested an Adherus</p> <p>13 product; correct?</p> <p>14 A That's correct.</p> <p>15 Q And you've never used any Adherus</p> <p>16 product; correct?</p> <p>17 A That's correct.</p> <p>18 Q And you've never seen a live surgical</p> <p>19 procedure being done with an Adherus product;</p> <p>20 correct?</p> <p>21 A That's correct.</p> <p>22 Q And you've never observed another</p>	<p style="text-align: right;">Page 224</p> <p>1 Just for the record, we don't have the</p> <p>2 video present in front of us when I answered that</p> <p>3 so --</p> <p>4 Q Yeah. Based on your recollection.</p> <p>5 A Yes. Thank you.</p> <p>6 MR. ALTHERR: Counsel, it's about</p> <p>7 quarter to 1:00. You plan on taking a lunch break</p> <p>8 any time soon?</p> <p>9 MR. HUGHES: Yeah, I was thinking if</p> <p>10 there's a --</p> <p>11 MR. ALTHERR: Is this a good place?</p> <p>12 MR. HUGHES: This is a fine stop. We</p> <p>13 can stop for lunch.</p> <p>14 MR. ALTHERR: Okay.</p> <p>15 THE WITNESS: We're off the record?</p> <p>16 THE VIDEOGRAPHER: This concludes disk</p> <p>17 number 2 of the video deposition of Dennis Rivet,</p> <p>18 M.D. The time is 12:41:31 p.m. We are now off</p> <p>19 the record.</p> <p>20 (Lunch recess -- 12:41 p.m.)</p> <p>21 (After recess -- 1:35 p.m.)</p> <p>22 THE VIDEOGRAPHER: This begins disk</p>
<p style="text-align: right;">Page 223</p> <p>1 surgeon using an Adherus product; correct?</p> <p>2 A I believe there's a surgeon using an</p> <p>3 Adherus product in the videos.</p> <p>4 Q So your -- your -- your view is limited</p> <p>5 to the one video, the Adherus AutoSpray Following</p> <p>6 Temporal Lobectomy video?</p> <p>7 A I don't know that -- who used in the</p> <p>8 AutoSpray preparation in those -- both those</p> <p>9 videos I observed.</p> <p>10 Q Okay.</p> <p>11 A Whoever the user was in those videos,</p> <p>12 and I assume the surgeon.</p> <p>13 Q Well, let's look at those videos --</p> <p>14 well, no. The Adherus AutoSpray preparation</p> <p>15 video, is that an actual surgery or is it a</p> <p>16 testing example?</p> <p>17 A My recollection is it is a testing</p> <p>18 example. It's a demonstration video, if you will.</p> <p>19 Q But not done on a patient or a live --</p> <p>20 A Correct.</p> <p>21 Q -- human or animal?</p> <p>22 A That's correct.</p>	<p style="text-align: right;">Page 225</p> <p>1 number 3 of the video deposition of Dennis Rivet,</p> <p>2 M.D. The time is approximately 1:35:03 p.m.</p> <p>3 We're now on the record.</p> <p>4 BY MR. HUGHES:</p> <p>5 Q Good afternoon, Dr. Rivet.</p> <p>6 During the break, were you able to</p> <p>7 determine when you were retained by Integra in</p> <p>8 this litigation?</p> <p>9 A Yes, the -- yes, date was April 20th --</p> <p>10 Q April 20th.</p> <p>11 A -- 2017.</p> <p>12 Q Okay. And, so, then when you requested</p> <p>13 to use the ET product around June or July 2017,</p> <p>14 that would have been after you were retained in</p> <p>15 this litigation; correct?</p> <p>16 A Correct.</p> <p>17 Q And I believe you previously testified</p> <p>18 that you wanted to use the product to inform your</p> <p>19 analysis or your opinion in this investigation; is</p> <p>20 that accurate?</p> <p>21 MR. ALTHERR: Object to the form.</p> <p>22 THE WITNESS: I wanted to use the</p>

<p style="text-align: right;">Page 226</p> <p>1 product because it was a new product that 2 interested me significantly, and I'd heard about 3 it, as we -- as we've discussed, prior to the 4 engagement on this -- on the matter. 5 BY MR. HUGHES: 6 Q Did you want to use the product to 7 inform your opinion in this litigation? 8 A Both that and to use the product to 9 inform myself regarding a new product. 10 Q But you have never used the product, 11 have you? 12 A Correct. 13 Q Did anyone from Integra imply that you 14 should request to use the product? 15 A No. 16 Q Did your counsel imply to you that you 17 should use the product? 18 MR. ALTHERR: All right. I'm going to 19 offer an objection here. First of all, you say 20 "your counsel." I assume you're referring to 21 plaintiffs' counsel. And if that -- if that's 22 what you are, we're going to object to him</p>	<p style="text-align: right;">Page 228</p> <p>1 A On legal engagements, yes. 2 Q What other rates do you charge in 3 nonlegal engagements? 4 A I've never set a rate on a nonlegal 5 engagement. 6 Q What was the last rate you had in a 7 nonlegal engagement? 8 A \$400 an hour for consulting, nonlegal. 9 Q Why do you charge more for legal 10 consulting than nonlegal consulting? 11 A Because I -- I -- I didn't set the 12 nonlegal rate. 13 Q Who set the nonlegal rate? 14 A The corporation. 15 Q Would that be the Elite service? 16 A No. 17 Q Which corporation? 18 A Medtronic. 19 Q Medtronic? 20 A Elite was legal. 21 Q Elite legal. 22 A I was referring to nonlegal consulting</p>
<p style="text-align: right;">Page 227</p> <p>1 answering any questions about what counsel and he 2 discussed on the grounds of work product. 3 THE WITNESS: No. 4 BY MR. HUGHES: 5 Q Looking at page 2 of your opening 6 report, that's Exhibit 4-1-1, 411, the footnote 7 identifies the rates you charge for consulting. 8 Do you see that? 9 A Correct. I do, yes. 10 Q And your standard consulting rate for 11 nontestifying activity is \$700 per hour; is that 12 accurate? 13 A Yes. 14 Q And \$1,400 per hour for a deposition; 15 is that correct? 16 A Yes. 17 Q And \$10,000 per day for trial; is that 18 accurate? 19 A Yes. 20 Q Are these the same rates that you 21 charge in other consulting engagement -- 22 engagements?</p>	<p style="text-align: right;">Page 229</p> <p>1 activities of which I've mentioned one only, and 2 that rate I didn't set. 3 Q The \$400 per hour, and that was with 4 Medtronic? 5 A That's correct. 6 Q And that was with nonlegal consulting? 7 A That's correct. 8 Q Okay. And who set your litigation 9 consulting rates? 10 A I did. 11 Q And this is what you charge all of your 12 litigation clients? 13 A Correct. 14 Q And do you charge the \$1,400 per hour 15 for preparation of a deposition, also? 16 A No. 17 Q Is this rate in line with what you're 18 aware other surgeons of your experience level 19 charge for their consulting rates? 20 A I don't know. 21 Q How did you set your rate? 22 A Somewhat arbitrarily in talking to my</p>

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1 colleagues. I didn't ask them their specific
 2 rate, but merely asked is it inappropriate.
 3 **Q And why do you charge more for**
 4 **deposition than nontestifying activities?**
 5 A There's more involved.
 6 **Q A deposition is more involved than**
 7 **nontestifying activities?**
 8 A Correct.
 9 **Q How is it more involved?**
 10 A It requires removing myself from my
 11 practice for two days.
 12 **Q For two days. So --**
 13 A In --
 14 **Q -- you --**
 15 A -- this --
 16 **Q -- charge --**
 17 A -- case --
 18 **Q In this --**
 19 A Yeah, in --
 20 **Q So you --**
 21 A This case --
 22 **Q -- charge --**

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1 A -- case. It involves. Excuse me. Go
 2 ahead. I'm not meaning --
 3 **Q I was going to say --**
 4 A -- to --
 5 **Q -- you --**
 6 A -- step --
 7 **Q -- charge --**
 8 A -- you.
 9 **Q -- \$1,400 per hour for your time in**
 10 **deposition even though it removes you from your**
 11 **practice for two days, but you don't charge a**
 12 **higher rate for deposition preparation?**
 13 A Correct.
 14 **Q How did you determine that \$10,000 per**
 15 **day at trial is an appropriate rate?**
 16 A My opinion.
 17 **Q What is your opinion based on?**
 18 A Talking to colleagues, the ways I'm
 19 able to in a nonscientific way assess the market
 20 rate for such activities.
 21 **Q So you believe \$10,000 per day is the**
 22 **market rate for your activities?**

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1 A I think it's a reasonable rate.
 2 **Q Let's move up in that same page to**
 3 **paragraph 4. If you look at the very last**
 4 **sentence in paragraph 4, My opinion with respect**
 5 **to these claims is that the selected concentration**
 6 **and visualization agent (or visualization agent**
 7 **having predetermined concentration) in the accused**
 8 **Adherus products causes a visually observable**
 9 **change indicating a predetermined thickness.**
 10 Do you see that?
 11 A Yes.
 12 **Q Which claims are you referring to when**
 13 **you say these claims?**
 14 A Multiple claims. Can we -- do you have
 15 a copy of the patents?
 16 **Q Well, do you identify the claims in**
 17 **your report that you are opining on?**
 18 A Yes. In that sentence I do not.
 19 **Q If you look at paragraph 2 at the**
 20 **bottom, you -- you list a understanding of the**
 21 **asserted claims in the case.**
 22 Do you see that?

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1 A The sentence begins, "I further
 2 understand that the method or process claims" --
 3 that sentence?
 4 **Q I don't see -- "I understand claims" --**
 5 **paragraph 2 --**
 6 A Yeah.
 7 **Q Yeah, the last part -- the last two**
 8 **sentences.**
 9 A Ah, I see. The last two sentences.
 10 "I understand the claims of '034, '566
 11 and '418 patents," that sentence and the one that
 12 follow it, yes.
 13 **Q Are these -- all of the claims that**
 14 **you're opining on in this report listed in the**
 15 **last two sentences of paragraph 2?**
 16 A (Witness reviews document.)
 17 Yes, I believe that's the case.
 18 **Q Then moving back to paragraph 4, the**
 19 **last --**
 20 A Okay.
 21 **Q -- sentence, so does this apply to any**
 22 **of the claims contained as limitations --**

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1 MR. ALTHERR: Object to form.
 2 BY MR. HUGHES:
 3 **Q -- that you're opining on in this**
 4 **report?**
 5 MR. ALTHERR: Object.
 6 THE WITNESS: I don't understand your
 7 question.
 8 BY MR. HUGHES:
 9 **Q So which claims are the ones you're**
 10 **opining on in this report?**
 11 **I'll strike that.**
 12 **In the last paragraph of page -- last**
 13 **sentence of paragraph 4, where in your report is**
 14 **your understanding of what a visualization agent**
 15 **entitles -- entails?**
 16 A I believe in page 7 the claim
 17 construction is excerpted and visualization agent
 18 is the first one.
 19 **Q And this is your understanding of what**
 20 **a visualization agent has been construed of?**
 21 A When you say "this," are you referring
 22 to that first bullet on page --

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1 **Q The first --**
 2 A -- 7?
 3 **Q -- bullet point on page 7.**
 4 A Yes.
 5 **Q And where in your report have you**
 6 **identified where in the DuraSeal product the**
 7 **visualization agent has been met?**
 8 A Can you rephrase your question?
 9 **Q In the report you identify and you**
 10 **speak about the DuraSeal product in relation to**
 11 **the asserted claims; is that correct?**
 12 A Yes.
 13 **Q And where do you identify how the**
 14 **visualization agent has been met by the DuraSeal**
 15 **product?**
 16 A I don't understand what you mean by how
 17 the visualization has been met.
 18 **Q Yeah.**
 19 A Those words I don't understand.
 20 **Q Strike that. We can get there in a**
 21 **second.**
 22 A Okay.

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1 **Q We'll come back to that question.**
 2 **Do you have any understanding of what**
 3 **visualization agent means other than the first**
 4 **bullet point listed on page 7?**
 5 A Within the context of this case, no,
 6 that's what I understand visualization agent to
 7 mean.
 8 **Q Within the context of this report, the**
 9 **meaning of what a visualization agent entails is**
 10 **contained in the first bullet point on page 7 of**
 11 **this report?**
 12 A I agree with that statement.
 13 **Q And did your discussions of Dr. Mays**
 14 **further elaborate upon your understanding of what**
 15 **a visualization agent entails?**
 16 A I don't -- I don't recall if our
 17 conversations -- I think your words were further
 18 elaborated? Can you rephrase it?
 19 **Q Yeah.**
 20 **Did your conversations with Dr. Mays**
 21 **further inform your opinion on what visualization**
 22 **agent means other than what's listed in the first**

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1 **bullet point on page 7?**
 2 A Yes, certainly we -- yes.
 3 **Q And did it inform the meaning of**
 4 **"visualization agent" or how the term**
 5 **"visualization agent" or that claim term is**
 6 **applied to various products?**
 7 MR. ALTHERR: Object to the form.
 8 THE WITNESS: Rephrase, please.
 9 BY MR. HUGHES:
 10 **Q Did your discussions with Dr. Mays**
 11 **further inform your understanding of the**
 12 **construction -- strike that.**
 13 **Do you understand when I say "claim**
 14 **construction," what I mean?**
 15 A Yes, I do.
 16 **Q That's when a court or somebody**
 17 **determines what the meaning of a word in a patent**
 18 **entails; is that accurate?**
 19 A That's my understanding as well.
 20 **Q So in the top -- in the first bullet**
 21 **point on page 7, you set forth a construction of**
 22 **visualization agent; is that correct?**

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1 A You said I set forth?

2 **Q Yeah, in your report.**

3 A I think we excerpt the claim

4 construction report.

5 **Q Okay.**

6 A I think it's verbatim from that report.

7 I don't know that I set it out.

8 **Q Well, I mean you put it in your report?**

9 A Correct. Yes. We've excerpted the

10 exact wording from the claim construction.

11 **Q Okay. And this is the construction you**

12 **applied in your opinions contained in this report?**

13 A Yes.

14 **Q And predetermined thickness -- well,**

15 **this -- the next terms in the series of bullet**

16 **points on page 7 to 8 and through page 9, all**

17 **within paragraph 19, these bullet points, are**

18 **these the claim constructions that you applied in**

19 **this report?**

20 A Yes.

21 **Q Then moving -- looking at page 9 after**

22 **the bullet points end, where you begin, I am not a**

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1 **chemist, a biochemist or designer of polymers, do**

2 **you see that paragraph?**

3 A Yes, I do.

4 **Q And you state, For purposes of this**

5 **report, I am assuming that the technical features**

6 **(e.g., what component of the products is a, quote,**

7 **reactive precursor species comprising**

8 **electrophilic functional groups), end quote.**

9 Do you see that?

10 A Yes.

11 **Q What -- so are you saying here that**

12 **you're relying upon Dr. Mays for an understanding**

13 **of what certain technical features mean?**

14 A Some of them, yes.

15 **Q And those are technical features within**

16 **the claim limitations?**

17 MR. ALTHERR: Object to the form.

18 THE WITNESS: Technical -- can you

19 distinguish claim limitations from some other

20 component of the claims?

21 BY MR. HUGHES:

22 **Q Well, no.**

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1 **So this -- this paragraph, you went**

2 **through the bullet points which are constructions**

3 **for various claim limitations; correct?**

4 A Okay. Understood.

5 **Q And now you're talking about if you --**

6 **the -- the sentence we were discussing earlier, it**

7 **concludes, I discussed the reasons set forth by**

8 **plaintiffs' expert Dr. Mays as set forth in the**

9 **infringement contentions.**

10 **So my -- my question is when you refer**

11 **to technical features in this -- in this sentence,**

12 **are you referring to claim limitations or aspects**

13 **of the accused products?**

14 A Both. I think we discuss both of them.

15 I wouldn't restrict them to either one of those by

16 itself.

17 **Q Okay. So when you say technical**

18 **features, for example, what component of the**

19 **product is a reactive precursor species comprising**

20 **electrophilic functional groups, did you rely upon**

21 **Dr. Mays for what the construction of the, quote,**

22 **reactive precursor species comprising**

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1 **electrophilic functional groups entails.**

2 MR. ALTHERR: Read that question back,

3 please.

4 (The Record was read as requested.)

5 MR. ALTHERR: Object to the form.

6 THE WITNESS: When you say

7 "construction," are you talking about manufacturer

8 or construction in the claim context?

9 BY MR. HUGHES:

10 **Q Claim construction.**

11 A I think that's a repeat of the last

12 question, if I understand it.

13 That, yes, I relied on components of

14 the claims and the claim construction with the

15 technical descriptions -- and that's an example --

16 that are beyond and outside my level of expertise.

17 **Q So that term in quotes there in the --**

18 **that begins, "the reactive precursor species," is**

19 **it your understanding that that's a claim term?**

20 A It is -- what -- what's a claim --

21 define "claim term," please.

22 **Q So at the end -- at the end of the**

<p style="text-align: right;">Page 242</p> <p>1 patent there's claims.</p> <p>2 A Uh-huh.</p> <p>3 Q You understand?</p> <p>4 And those claims define what is covered</p> <p>5 by that patent. Do you understand?</p> <p>6 A Understood.</p> <p>7 Q And those claims recite a number of</p> <p>8 claim terms or claim elements.</p> <p>9 Do you understand?</p> <p>10 A Yes.</p> <p>11 Q So this quote here, do you understand</p> <p>12 that to be one of the claim terms in one of the</p> <p>13 asserted claims in this litigation?</p> <p>14 A Yes, I do.</p> <p>15 Q And are you relying upon Dr. Mays for</p> <p>16 an understanding of the construction of what that</p> <p>17 claim term is?</p> <p>18 A Yes, I believe so.</p> <p>19 Q And is this what you refer to as a</p> <p>20 technical feature in that sentence?</p> <p>21 A It's an example of one, yes.</p> <p>22 Q So the claim terms of the asserted</p>	<p style="text-align: right;">Page 244</p> <p>1 MR. HUGHES: Strike that.</p> <p>2 BY MR. HUGHES:</p> <p>3 Q For other technical terms that you do</p> <p>4 not rely upon Dr. Mays for the understanding of</p> <p>5 their construction, you rely upon the court's</p> <p>6 construction; is that accurate?</p> <p>7 MR. ALTHERR: Object to the form.</p> <p>8 THE WITNESS: The -- the -- I don't</p> <p>9 think I understand the question. The</p> <p>10 understanding of the terms and the claims, my --</p> <p>11 my ability to define them and opine on them</p> <p>12 sometimes requires my consulting with Dr. Mays.</p> <p>13 There are other terms that do not in -- in the</p> <p>14 claims.</p> <p>15 BY MR. HUGHES:</p> <p>16 Q For the claim terms that do not require</p> <p>17 your consultation with Dr. Mays, how did you</p> <p>18 determine the meaning of those claim terms?</p> <p>19 A Some of the -- as -- as listed on</p> <p>20 page 7 and 8, some of them are in the claim</p> <p>21 constructions. There are other components in the</p> <p>22 claims that I don't think are in the report from</p>
<p style="text-align: right;">Page 243</p> <p>1 claims can be technical features that you're</p> <p>2 relying upon Dr. Mays for their construction?</p> <p>3 MR. ALTHERR: Object to the form.</p> <p>4 THE WITNESS: In certain circumstances</p> <p>5 related to polymer chemistry and phrase -- terms</p> <p>6 such as this, yes. There are other technical</p> <p>7 features, as I've stated previously, that I do not</p> <p>8 need to rely on Dr. Mays.</p> <p>9 BY MR. HUGHES:</p> <p>10 Q So you -- some technical features you</p> <p>11 rely upon Dr. Mays for an understanding of the</p> <p>12 claim construction --</p> <p>13 A That's correct.</p> <p>14 Q -- is that accurate?</p> <p>15 And for other technical features, you</p> <p>16 do not rely upon Dr. Mays for a claim</p> <p>17 construction; is that accurate?</p> <p>18 A It is.</p> <p>19 Q And for the terms -- for the claim</p> <p>20 terms you do not rely upon Dr. Mays for, you rely</p> <p>21 upon the court for; correct?</p> <p>22 MR. ALTHERR: Object to the form.</p>	<p style="text-align: right;">Page 245</p> <p>1 Judge Burke on August 18th, and I don't need to</p> <p>2 rely -- I shouldn't say don't need to rely -- that</p> <p>3 I didn't rely on the court or doctor -- the court</p> <p>4 meaning Magistrate Burke's ruling on August 18th.</p> <p>5 Q What terms in the asserted claims have</p> <p>6 you opined on -- what terms in the asserted claims</p> <p>7 have you applied in your opinion where you did not</p> <p>8 rely upon either the court's construction or</p> <p>9 Dr. Mays?</p> <p>10 Where are those terms located in your</p> <p>11 report?</p> <p>12 A I don't know that the terms themselves</p> <p>13 are located. The -- when I say "terms," I mean</p> <p>14 the elements of the claims, and the claims are</p> <p>15 listed. So there's language that is not included.</p> <p>16 My understanding is that there are --</p> <p>17 there are components of the claims that are not</p> <p>18 listed on the construction and that don't involve,</p> <p>19 in my opinion, technical features that are</p> <p>20 detailed chemistry, et cetera. And those are the</p> <p>21 ones I would say -- and if you gave me an</p> <p>22 example . . .</p>

<p style="text-align: right;">Page 246</p> <p>1 Q Okay. Well, let's --</p> <p>2 A If we --</p> <p>3 Q -- look --</p> <p>4 A -- go through a claim, for example.</p> <p>5 Q Sure.</p> <p>6 Well, let's look at paragraph 20 of</p> <p>7 your report.</p> <p>8 A Paragraph 20. Okay.</p> <p>9 Q It identifies claim 1 of the '034</p> <p>10 patent. Do you see that?</p> <p>11 A Yes, I do.</p> <p>12 Q And the second step says -- second</p> <p>13 sentence addresses steps of preparing a</p> <p>14 composition including the mixing of components,</p> <p>15 and it lists a statement there.</p> <p>16 Do you see that?</p> <p>17 A "'034 patent is directed to a method of</p> <p>18 preparing a composition suitable for coating</p> <p>19 tissue of a patient with a composition that has</p> <p>20 certain properties" is the sentence you're --</p> <p>21 Q Correct.</p> <p>22 A Yes.</p>	<p style="text-align: right;">Page 248</p> <p>1 Do you see that?</p> <p>2 A Yes.</p> <p>3 Q And your construction of visualization</p> <p>4 agent, you're relying upon the court for that;</p> <p>5 correct?</p> <p>6 A Agreed.</p> <p>7 Q And for -- the visualization agent</p> <p>8 causes a visually observable change, for what a</p> <p>9 visually observable change means, are you relying</p> <p>10 on the court or Dr. Mays or your own</p> <p>11 understanding?</p> <p>12 A No, I think on page 7 I've listed that</p> <p>13 that's one of the terms I'm relying the --</p> <p>14 Q Observable change --</p> <p>15 A -- con- --</p> <p>16 Q Okay.</p> <p>17 A -- -struction, yes.</p> <p>18 Q And --</p> <p>19 A I guess you said additional words.</p> <p>20 So observable change is listed, but,</p> <p>21 yes, I'm relying on the court.</p> <p>22 Q And for the determine -- predetermined</p>
<p style="text-align: right;">Page 247</p> <p>1 Q Any of the terms listed in this</p> <p>2 paragraph -- are they terms that you determined</p> <p>3 the meaning for without relying upon the court's</p> <p>4 construction or Dr. Mays?</p> <p>5 A I'd have -- I'd have to go back and</p> <p>6 look at the entire claim construction and that --</p> <p>7 from August and see are any of those terms</p> <p>8 considered in it.</p> <p>9 Q Okay. Well, maybe we can have a little</p> <p>10 more of a -- of a focused look.</p> <p>11 So looking at paragraph 21 --</p> <p>12 A Okay.</p> <p>13 Q -- addressing claim 16 of the '034</p> <p>14 patent --</p> <p>15 A Uh-huh.</p> <p>16 Q -- where it states, The sep -- The step</p> <p>17 of selecting a concentration of visaliza- --</p> <p>18 visualization agent such that the visualization</p> <p>19 agent causes a visually observable change</p> <p>20 indicating a predetermined thickness the</p> <p>21 composition had been formed in the tissue [as</p> <p>22 read].</p>	<p style="text-align: right;">Page 249</p> <p>1 thickness, you're relying upon the court's</p> <p>2 construction on page 7?</p> <p>3 A Yes, sir.</p> <p>4 Q Are you aware that the accused Adherus</p> <p>5 products have air bubbles within the hydrogels</p> <p>6 that are formed?</p> <p>7 A Yes.</p> <p>8 Q Are air bubbles a visualization agent</p> <p>9 under your con- -- under the construction you're</p> <p>10 using in this report?</p> <p>11 A The visualization agent definition</p> <p>12 states a substance or material that is detectable</p> <p>13 by the human eye and then imparts a color or</p> <p>14 obscures the optical clarity. And I don't believe</p> <p>15 air is visible to the human eye, and in the claim</p> <p>16 construction that was discussed.</p> <p>17 Q So in this report -- your opening</p> <p>18 report, you're not considering air bubbles to be a</p> <p>19 visualiza- -- visualization agent; is that correct?</p> <p>20 A That's correct.</p> <p>21 Q Are you -- in your opening report, are</p> <p>22 you considering a dye or combinations of dyes to</p>

<p style="text-align: right;">Page 250</p> <p>1 be a visualization agent?</p> <p>2 A Yes, I believe a dye or a combination</p> <p>3 of dyes meets the definition of a visualization</p> <p>4 agent.</p> <p>5 Q And for shorthand today, can we just</p> <p>6 use dye singular? Is that okay?</p> <p>7 A Sounds great.</p> <p>8 Q So in the opinion you set forth in this</p> <p>9 report, are you considering a vis- -- you do not</p> <p>10 consider visual- -- visualization agent to</p> <p>11 entail -- entitle [verbatim] air bubbles; correct?</p> <p>12 A Correct.</p> <p>13 Q But you do consider a visualization</p> <p>14 agent to entail a dye; correct?</p> <p>15 A I would phrase it as I would consider a</p> <p>16 dye a visualization agent.</p> <p>17 Q Okay. Do you consider air bubbles plus</p> <p>18 a dye a visualization agent?</p> <p>19 I can strike that.</p> <p>20 In this report you submitted on</p> <p>21 August 24th, 2017, in the -- that -- that form the</p> <p>22 opinions -- your opinions, did you consider a dye</p>	<p style="text-align: right;">Page 252</p> <p>1 mixture -- in this case your question was air and</p> <p>2 visualization -- a dye, they're going to be</p> <p>3 visible to the human eye and impart a color and,</p> <p>4 therefore, will meet the definition of a</p> <p>5 visualization agent, so I would consider that.</p> <p>6 Q Where in your opinion did you expressly</p> <p>7 state forth your -- your -- your -- strike that.</p> <p>8 Where in your report did you expressly</p> <p>9 provide your opinions that a dye plus air bubbles</p> <p>10 meets the visualization agent requirement?</p> <p>11 MR. ALTHERR: Object to the form.</p> <p>12 THE WITNESS: I don't -- I don't know</p> <p>13 that it's in my report what you just stated.</p> <p>14 BY MR. HUGHES:</p> <p>15 Q So the report you submitted on</p> <p>16 August 24, 2017, doesn't apply a dye plus</p> <p>17 visual -- plus air bubbles to equal a</p> <p>18 visualization agent to the accused products; is --</p> <p>19 MR. ALTHERR: Object --</p> <p>20 BY MR. HUGHES:</p> <p>21 Q -- that --</p> <p>22 MR. ALTHERR: -- to the --</p>
<p style="text-align: right;">Page 251</p> <p>1 plus air bubbles to meet the visualization agent</p> <p>2 requirement of the claims?</p> <p>3 A I don't quite understand. So you're --</p> <p>4 no, in the sense that once one element of</p> <p>5 something has met the definition for visualization</p> <p>6 agent, I believe it's a visualization agent.</p> <p>7 If you add nonvisualization agents with</p> <p>8 a visualization agent, you still have present a</p> <p>9 visualization agent.</p> <p>10 Q So you considered a dye alone a</p> <p>11 visual -- a visualization agent; correct?</p> <p>12 A Yes.</p> <p>13 Q But you did not consider air bubbles</p> <p>14 alone a visualization agent; correct?</p> <p>15 A Correct.</p> <p>16 Q And you're saying you did not consider</p> <p>17 air bubbles plus a dye to be the visualization</p> <p>18 agent?</p> <p>19 A No, I don't think I said that.</p> <p>20 I think any visualization agent --</p> <p>21 if -- if -- if there's a mixture of two things,</p> <p>22 one of which is a visualization agent, the</p>	<p style="text-align: right;">Page 253</p> <p>1 BY MR. HUGHES:</p> <p>2 Q -- correct?</p> <p>3 MR. ALTHERR: -- form.</p> <p>4 THE WITNESS: Can you rephrase the</p> <p>5 question?</p> <p>6 BY MR. HUGHES:</p> <p>7 Q Your opening report does not contain an</p> <p>8 opinion that a dye plus air bubbles equals a</p> <p>9 visualization agent; is that correct?</p> <p>10 MR. ALTHERR: Object to the form.</p> <p>11 THE WITNESS: I do not think I</p> <p>12 commented or opined on that specific question.</p> <p>13 BY MR. HUGHES:</p> <p>14 Q And in your report on August 24th,</p> <p>15 2017 -- your opening report, you didn't apply that</p> <p>16 specific question, as you put it, to the accused</p> <p>17 products, did you?</p> <p>18 MR. ALTHERR: Object to the form.</p> <p>19 THE WITNESS: I don't think I can --</p> <p>20 correct. The -- the question is -- to me it is</p> <p>21 semantic in that if a number of things contain a</p> <p>22 visualization agent, they've met the definition.</p>

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1 BY MR. HUGHES:
 2 **Q So in your report on August 17**
 3 **[verbatim] -- your opening report, you do provide**
 4 **the opinions that a dye equals visualization**
 5 **agent; correct?**
 6 A I think I defined -- I excerpted the
 7 court's definition of what -- a visualization
 8 agent and agreed with that as a definition.
 9 **Q In this report you opine that the**
 10 **accused products are infringed by various asserted**
 11 **claims; correct?**
 12 A Did you say "various asserted claims";
 13 is that what --
 14 **Q Yeah.**
 15 A Yes, I agree with that.
 16 **Q And some of these claims, if not all of**
 17 **them, require a visualization agent; is that**
 18 **accurate?**
 19 A Correct.
 20 **Q So in this report your position is that**
 21 **you do expressly apply a dye being a visualization**
 22 **agent to formulate an opinion of infringement**

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1 **regarding the accused products; correct?**
 2 A I don't think dye is in the report,
 3 but --
 4 **Q So -- that's a good point. So when**
 5 **you -- let's look at the Adherus product, for**
 6 **example -- the accused Adherus products.**
 7 **This report provides the opinion that**
 8 **they provide -- they entail a visual -- a**
 9 **visualization agent; correct?**
 10 A Yes.
 11 **Q Where in this report does it set forth**
 12 **that the accused Adherus product entail a**
 13 **visualization agent?**
 14 A Would you rephrase that?
 15 **Q Where in your report do you opine the**
 16 **accused Adherus products have the visualization --**
 17 **meet the vis- -- visualization agent requirement?**
 18 A (Witness reviews document.)
 19 I think one example is on page 7, and
 20 that's the continuation of paragraph 18. I
 21 believe this is answering your question, but the
 22 sentence begins, "My opinion."

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1 **Q Uh-huh.**
 2 A My opinion with respect to these claims
 3 is that the selected concentration of
 4 visualization agent or visualization agent having
 5 a predetermined concentration in the accused
 6 Adherus products, and it goes on.
 7 **Q In your opinion here what of the**
 8 **accused Adherus products meets the visualization**
 9 **agent requirement?**
 10 A The fact that it contains a
 11 visualization agent in it.
 12 **Q What is the visualization agent in the**
 13 **accused products?**
 14 A A coloring agent, a dye. We can use
 15 "dye."
 16 **Q Where in your opinion do you say that**
 17 **the visualization agent is a dye?**
 18 A I don't think I do.
 19 **Q And in your opinion here in**
 20 **paragraph 18, does this entail -- does a**
 21 **visualization agent plus bubbles entail -- pardon**
 22 **me. Strike that.**

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1 **In your opinion we're talking about in**
 2 **paragraph 18, would a dye plus bubbles entail a**
 3 **visualization agent?**
 4 MR. ALTHERR: Objection.
 5 THE WITNESS: We've defined "dye." I
 6 think we've agreed -- I've stated that dye is a
 7 visualization agent. It meets the definition of
 8 visualization agent; therefore, anything placed
 9 into a hydrogel that has something that meets the
 10 visualization agent, will meet the definition.
 11 I mean, another way to phrase that
 12 would be if you were to include any substance that
 13 did not meet the visualization agent definition --
 14 in this case you've suggested air -- and you
 15 include it with the visualization agent and put it
 16 in a product, it will meet the definition.
 17 So that's why I -- it's -- it feels --
 18 BY MR. HUGHES:
 19 **Q I'm not trying to challenge what your**
 20 **opinion is right now, Dr. Rivet. I'm just trying**
 21 **to identify where in your report you state**
 22 **opinions or don't state opinions.**

<p style="text-align: right;">Page 258</p> <p>1 A Uh-huh.</p> <p>2 Q So the question is anywhere in your</p> <p>3 report do you state the opinion that a dye plus</p> <p>4 air bubbles meets the visualization agent</p> <p>5 requirement?</p> <p>6 MR. ALTHERR: Object to the form.</p> <p>7 THE WITNESS: I don't think that's in</p> <p>8 the report.</p> <p>9 BY MR. HUGHES:</p> <p>10 Q Okay. Moving to paragraph 35 --</p> <p>11 actually, before I get to paragraph 35, is there</p> <p>12 anywhere else in the report -- paragraph 4 of the</p> <p>13 report, Dr. Rivet. Your statement of</p> <p>14 visualization agent here, this comports with your</p> <p>15 statement of visualization agent in paragraph 18</p> <p>16 we were just discussing?</p> <p>17 A (Witness reviews document.)</p> <p>18 So does paragraph 4 -- would you</p> <p>19 rephrase -- what is the relation -- you're asking</p> <p>20 what the relationship of my wording in paragraph 4</p> <p>21 to the sentence that we talked about in</p> <p>22 paragraph --</p>	<p style="text-align: right;">Page 260</p> <p>1 A I'm there. Yes, causes visually</p> <p>2 observable change.</p> <p>3 Q Where in the report do you identify</p> <p>4 what the visibly observable change is in the</p> <p>5 accused Adherus products that meets this</p> <p>6 limitation?</p> <p>7 A I believe it falls under observable</p> <p>8 change, bullet number 3 on page 7, excerpted from</p> <p>9 page 37 of the claim construction.</p> <p>10 Q And that's for your understanding of</p> <p>11 what observable change means; correct?</p> <p>12 A It is.</p> <p>13 Q Now, where in the report have you</p> <p>14 identified what in the accused Adherus products or</p> <p>15 the use of the accused Adherus products meets that</p> <p>16 observable change requirement?</p> <p>17 A Would you rephrase that, please, or --</p> <p>18 or repeat it at least?</p> <p>19 Q Sure.</p> <p>20 Claim 21 addresses an observable change</p> <p>21 requirement -- pardon me.</p> <p>22 Paragraph 21 addresses claim 16 of the</p>
<p style="text-align: right;">Page 259</p> <p>1 Q The contents of the opinion expressed</p> <p>2 in paragraph 4 --</p> <p>3 A Okay.</p> <p>4 Q -- is that the same opinion -- is</p> <p>5 that -- is there anything antithetical of the</p> <p>6 opinion established in paragraph 18?</p> <p>7 A (Witness reviews document.)</p> <p>8 I do not see anything antithetical. In</p> <p>9 fact, the last sentence of paragraph 4 seems</p> <p>10 extremely similar. Reading the sentence, My</p> <p>11 opinion with respect to these claims is that the</p> <p>12 selected concentration of visualization agent (or</p> <p>13 visualization agent having a predetermined</p> <p>14 concentration) in the accused Adherus product</p> <p>15 causes a visually observable change, is very</p> <p>16 similar to the sentence in paragraph 4.</p> <p>17 Q Okay. Moving back to paragraph 21 we</p> <p>18 were discussing earlier. You mention a visually</p> <p>19 observable change in the third line of</p> <p>20 paragraph 21.</p> <p>21 A Paragraph 21?</p> <p>22 Q Yes, the visually observable change.</p>	<p style="text-align: right;">Page 261</p> <p>1 '034 patent which entails an observable change</p> <p>2 requirement; correct?</p> <p>3 A Yes.</p> <p>4 Q So the question is where in the report</p> <p>5 do you identify where that observable change</p> <p>6 requirement is met by the accused Adherus</p> <p>7 products?</p> <p>8 A (Witness reviews document.)</p> <p>9 I'll ask you to repeat it. I'm sorry</p> <p>10 to ask a third time. I want to make sure I have</p> <p>11 addressed it. Would you mind reading back the</p> <p>12 question?</p> <p>13 Q So maybe we can focus a little. In</p> <p>14 paragraph 35 --</p> <p>15 A Okay.</p> <p>16 Q -- do you identify anywhere in this</p> <p>17 paragraph where you met -- where you opine the</p> <p>18 observable change requirement has been met by the</p> <p>19 accused Adherus products?</p> <p>20 A (Witness reviews document.)</p> <p>21 The sentence that says, The green color</p> <p>22 of the Adherus product allows the user to gauge</p>

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1 the thickness of the coating as it is being
2 applied.
3 It has to do with the observable change
4 that occurs in the Adherus product specifically.
5 **Q But do you state that the green color**
6 **as it's being applied is the observable change?**
7 A No. I go on to say in the sentence
8 that begins, "My own observations," at the point
9 where -- "at the point when there is a uniform,
10 even coating changing the color of the target site
11 from the natural tissue color to an even green
12 color," that sentence also addresses the
13 observable change the user witnesses.
14 **Q And then it goes on to say, "the user**
15 **has reached the predetermined thickness of 1 to 2**
16 **millimeters."**
17 **Do you see that?**
18 A Yes, same sentence.
19 **Q So is the predetermined thickness**
20 **that's required by the claims 1 to 2 millimeters?**
21 A Yes, that's exactly what it says.
22 **Q Is there anywhere in paragraph 35 of**

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1 the report that discuss -- that opines upon a
2 correlation between an observable change and the
3 predetermined thickness?
4 A Yes, I think in that sentence -- that
5 same sentence.
6 **Q That begins, "My own observations"?**
7 A That's correct.
8 **Q And I think that's -- is that the last**
9 **sentence in the paragraph, I believe?**
10 A Yes, it is.
11 **Q So that sentence contains your opinion**
12 **that there's a correlation between an observable**
13 **change and a predetermined thickness?**
14 A Correct. Just to say verbatim, at this
15 point coating obs -- quote, at this point the
16 coating obscures the sutures, subjacent tissue
17 plane or microvasculature indicating the user has
18 reached the predetermined thickness of 1 to
19 2 millimeters specified in the Adherus products I
20 have used, end quote.
21 Yes, I think that answers what we --
22 **Q And is --**

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1 A -- just (unintelligible) --
2 **Q -- is this the only place in your**
3 **report where you opine upon a correlation between**
4 **an observable change and predetermined thickness?**
5 MR. ALTHERR: Object to the form.
6 THE WITNESS: I think in paragraph 38 I
7 also excerpted an IFU that reads, quote, The
8 HyperBranch Adherus products respective
9 instructions (IFUs) require the surgeon to do the
10 following.
11 And then from the IFU it says, Form a
12 composition and apply it on the tissue of a
13 patient such that a visually observable green
14 color occurs on the tissue that at least obscures
15 a suture thus indicating a predetermined
16 thickness.
17 **Q And this is your opinion that there's a**
18 **correlation between the observable change and the**
19 **predetermined thickness?**
20 A Yes.
21 **Q Does this -- this is the second bullet**
22 **point on -- in paragraph 37 that you're referring**

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1 to?
2 A The -- what I just read was the -- came
3 from paragraph 38.
4 **Q Pardon me.**
5 **So in paragraph 38 the bullet point,**
6 **that's your opinion on the -- that there's a**
7 **correlation between an observable change and a**
8 **predetermined thickness; correct?**
9 A Well, the bullet point is an excerpted
10 piece of wording from the IFU --
11 **Q Okay.**
12 A -- but I have stated that that's --
13 there were -- that the instructions require the
14 surgeon to do that.
15 The paragraph you also pointed out, the
16 second one in 37, is although similar -- not
17 exactly the same wording, also describes the same
18 thing.
19 **Q The second bullet point in paragraph 37**
20 **or the third -- the bullet point in third --**
21 **paragraph 38, do you express an opinion that a**
22 **color change is the observable change?**

<p style="text-align: right;">Page 266</p> <p>1 A Yes, the color change -- correct.</p> <p>2 Q Where -- where do you -- where does the</p> <p>3 report provide the opinion that there's -- a color</p> <p>4 change meets the -- the observable change?</p> <p>5 A I think those two paragraphs we just</p> <p>6 discussed do that.</p> <p>7 Q And where in the paragraph is that</p> <p>8 located -- where in either of the two paragraphs</p> <p>9 is that located?</p> <p>10 A Sure. Reading 38 again first, Each of</p> <p>11 the HyperBranch Adherus products respective IFUs</p> <p>12 require the surgeon to do the following: form a</p> <p>13 composition applied on the tissue of the patient</p> <p>14 such that a visually observable green color occurs</p> <p>15 on the tissue.</p> <p>16 And it continues on.</p> <p>17 Q So the observable green color occurring</p> <p>18 on the tissue in the second line of the bullet</p> <p>19 point there --</p> <p>20 MR. ALTHERR: Object to the form.</p> <p>21 Counsel, again this is the second time</p> <p>22 you've stopped him before he finished answering</p>	<p style="text-align: right;">Page 268</p> <p>1 I think, as we've also discussed, going to 37, the</p> <p>2 second paragraph -- we can read it, but it --</p> <p>3 respective IFU -- again I'm going to the last</p> <p>4 sentence leading into the bullets, Respective IFUs</p> <p>5 require the surgeon to do the following.</p> <p>6 And now I'll skip to the second bullet:</p> <p>7 Mixing the components in a predetermined</p> <p>8 concentration of a visualization so that when</p> <p>9 mixed the visualization agent in the composition</p> <p>10 will indicate a predetermined thickness of the</p> <p>11 hydrogel.</p> <p>12 Skipping ahead, "on the tissue surface</p> <p>13 by having the green color at least obscure the</p> <p>14 fine epidural vasculature."</p> <p>15 I've skipped some words, but for</p> <p>16 meaning, yes.</p> <p>17 Q So the observable change is the</p> <p>18 hydrogel on the tissue surface having a green</p> <p>19 color at least obscure the fine epidural</p> <p>20 vasculature?</p> <p>21 A That's right. That's one example.</p> <p>22 Q Apart from these two bullet points, are</p>
<p style="text-align: right;">Page 267</p> <p>1 his question.</p> <p>2 MR. HUGHES: I wasn't aware he was not</p> <p>3 finished answering his question.</p> <p>4 BY MR. HUGHES:</p> <p>5 Q Dr. Rivet, were you finished answering</p> <p>6 the question?</p> <p>7 A I'm done. Thank you.</p> <p>8 Q So in paragraph 38, the second line --</p> <p>9 I think that's what we were just referring to --</p> <p>10 that states -- well, it begins in the first line,</p> <p>11 A visually observable green color occurs on the</p> <p>12 tissue.</p> <p>13 Is that what you were just referring</p> <p>14 to?</p> <p>15 A "A visually observable green color" is</p> <p>16 from the first line of the excerpted bullet, yes.</p> <p>17 Q And that's the support for your opinion</p> <p>18 that a color change meets the observable change as</p> <p>19 required by the patents?</p> <p>20 A Among --</p> <p>21 MR. ALTHERR: Object to the form.</p> <p>22 THE WITNESS: Among other things, yes.</p>	<p style="text-align: right;">Page 269</p> <p>1 there other examples of a color change meeting the</p> <p>2 requirement of an observable change?</p> <p>3 I'll restate that.</p> <p>4 A Thanks.</p> <p>5 Q The asserted claims require an</p> <p>6 observable change; correct?</p> <p>7 A Yes.</p> <p>8 MR. ALTHERR: Object to the form.</p> <p>9 BY MR. HUGHES:</p> <p>10 Q And does this report provide any other</p> <p>11 opinions other than the ones in 30 -- paragraph 37</p> <p>12 and 38 that a color change in the accused products</p> <p>13 would meet the required observable change?</p> <p>14 A Going back to paragraph 35, we've --</p> <p>15 again, we've covered this paragraph, but middle of</p> <p>16 the paragraph sentence beginning, The green color</p> <p>17 of the Adherus products allows a user to gauge the</p> <p>18 thickness of the coating as it is being applied.</p> <p>19 My own observations and the HyperBranch videos</p> <p>20 demonstrate that the user understands to stop</p> <p>21 applying the Adherus product at the point where</p> <p>22 there is a uniform, even coating changing the</p>

<p style="text-align: right;">Page 270</p> <p>1 color of the target site from natural tissue color</p> <p>2 to an even green color, and at this point coating</p> <p>3 obscures the sutures, subjacent tissue plane or</p> <p>4 microvasculature.</p> <p>5 That's a summary, and it talks about a</p> <p>6 couple different color -- a couple of different</p> <p>7 effects of applying a coloring, you know, a</p> <p>8 visualization agent, but that's another location</p> <p>9 in the report.</p> <p>10 Q Do any of these areas talk about a</p> <p>11 change in color of the hydrogel itself?</p> <p>12 Rephrasing it a little bit, does your</p> <p>13 opinion provide an express example of a change in</p> <p>14 color of the hydrogel itself meeting the</p> <p>15 observable change requirement?</p> <p>16 MR. ALTHERR: Object to the form.</p> <p>17 THE WITNESS: The only thing we're</p> <p>18 discussing -- the only thing it is talking about</p> <p>19 is the observable change of the hydrogel.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q So when the hydrogel obscures a</p> <p>22 microvascular underneath, that's a change in color</p>	<p style="text-align: right;">Page 272</p> <p>1 A I -- again, we -- we -- I think we did</p> <p>2 cover air bubbles a --</p> <p>3 Q We --</p> <p>4 A -- very --</p> <p>5 Q -- did.</p> <p>6 A -- short time. But -- but I'll say</p> <p>7 again, not that I'm aware of in the report. And</p> <p>8 correct me if I'm missing . . .</p> <p>9 Q The --</p> <p>10 A If your point is -- excuse me. I'm</p> <p>11 sorry to talk over you.</p> <p>12 If your point is that there's an</p> <p>13 element where I did mention it, please. But I do</p> <p>14 not believe a discussion of air bubbles obscuring</p> <p>15 is mentioned.</p> <p>16 Q Thank you.</p> <p>17 Looking at paragraph 35, we've been</p> <p>18 talking about this paragraph where it relates to</p> <p>19 your provided opinions on a change in color and a</p> <p>20 correlation of a change in color and a</p> <p>21 predetermined thickness.</p> <p>22 Is that an accurate statement?</p>
<p style="text-align: right;">Page 271</p> <p>1 of the hydrogel?</p> <p>2 A Yes. The mechanism of obscuration of</p> <p>3 sutures, subjacent tissue plane or microvascular</p> <p>4 is a change in the hydrogel color intensity,</p> <p>5 clarity, et cetera, as it is applied.</p> <p>6 Q The color of the hydrogel changes, and</p> <p>7 that's the observable change as it obscures</p> <p>8 sutures; is that your opinion?</p> <p>9 MR. ALTHERR: Object to the form.</p> <p>10 THE WITNESS: The clarity and</p> <p>11 appearance of the hydrogel color changes during</p> <p>12 the application which results in -- you've stated</p> <p>13 one example but other visual changes.</p> <p>14 BY MR. HUGHES:</p> <p>15 Q In your report do you state anywhere</p> <p>16 that air bubbles are involved in the hydrogel</p> <p>17 obscuring the suture knots or any -- any of the</p> <p>18 other changes we're discussing?</p> <p>19 A I do not believe I state that air</p> <p>20 bubbles do that in the report.</p> <p>21 Q Does this report address anywhere air</p> <p>22 bubbles obscuring suture knots?</p>	<p style="text-align: right;">Page 273</p> <p>1 A Yes.</p> <p>2 Q And your opinion provided in the report</p> <p>3 about a change in color or a change in color --</p> <p>4 strike that.</p> <p>5 Your -- the opinion provided in your</p> <p>6 report about a change in color or about an</p> <p>7 observable change correlated with a predetermined</p> <p>8 thickness.</p> <p>9 Did you base those opinions on your</p> <p>10 discussions with your VCU colleagues that you</p> <p>11 identify here on page -- paragraph 34 -- 35?</p> <p>12 MR. ALTHERR: Object to the form.</p> <p>13 THE WITNESS: It's hard to separate</p> <p>14 out -- I have a -- I'm unable to separate out my</p> <p>15 opinions on the specific color change topic right</p> <p>16 now from my discussions regarding the products.</p> <p>17 BY MR. HUGHES:</p> <p>18 Q You remember this morning we talked</p> <p>19 about your discussions with the series of people</p> <p>20 at VCU.</p> <p>21 A Yes, I do.</p> <p>22 Q So let's keep that group of people in</p>

<p style="text-align: right;">Page 274</p> <p>1 mind for a second.</p> <p>2 A Yes.</p> <p>3 Q In your discussions with your</p> <p>4 colleagues at VCU, did you expressly discuss the</p> <p>5 color change of the Adherus product as it's being</p> <p>6 applied with them?</p> <p>7 A I do not recall the specifics of what</p> <p>8 about the color of the Adherus product we</p> <p>9 discussed with the group of people as I think I've</p> <p>10 answered previously today, but those discussions</p> <p>11 certainly factor into my opinion of which the</p> <p>12 opinion regarding the color change resulting in a</p> <p>13 predetermined thickness is one of them.</p> <p>14 Q But you can't point to any specific</p> <p>15 discussion with a colleague at VCU where they</p> <p>16 informed you they use a color change to correlate</p> <p>17 with a predetermined thickness; is that accurate?</p> <p>18 A That is correct. I cannot.</p> <p>19 Q And you cannot point to any specific</p> <p>20 discussion with your colleagues at VCU where they</p> <p>21 can point to any observable change being</p> <p>22 correlated for predetermined thickness; is that</p>	<p style="text-align: right;">Page 276</p> <p>1 colleague at VCU where they informed you that they</p> <p>2 use a color change to correlate the predetermined</p> <p>3 thickness; is that accurate?</p> <p>4 A I agree with that statement.</p> <p>5 Q And that applies to your entire report,</p> <p>6 not just paragraph 35; correct?</p> <p>7 A Yes, I agree with that statement.</p> <p>8 Q Other than paragraph 35 and 36 and</p> <p>9 paragraph 37 and 38 -- so excluding those four</p> <p>10 paragraphs -- is there anywhere else in the report</p> <p>11 where you express the opinion that an observable</p> <p>12 change is correlated with a predetermined</p> <p>13 thickness in the accused Adherus products?</p> <p>14 A Okay. Let me take a look.</p> <p>15 (Witness reviews document.)</p> <p>16 So in paragraph 31 and 32, the -- the</p> <p>17 parts that are excerpted again discuss this. In</p> <p>18 the 31 paragraph, for existence -- for example,</p> <p>19 the -- under the excerpted part Treatment</p> <p>20 Delivery, line 19, Once a green sealant begins to</p> <p>21 form on the piece of gauze, stop depressing the</p> <p>22 syringe pusher assembly. And then 20, While</p>
<p style="text-align: right;">Page 275</p> <p>1 accurate?</p> <p>2 MR. ALTHERR: Object to the form.</p> <p>3 THE WITNESS: That's correct. I</p> <p>4 cannot.</p> <p>5 BY MR. HUGHES:</p> <p>6 Q And the two statements we just said,</p> <p>7 that applies to your entire opinion in this</p> <p>8 report, correct, not just paragraph 35?</p> <p>9 MR. ALTHERR: Object to form.</p> <p>10 THE WITNESS: I think -- please clarify</p> <p>11 the -- when you say "two statements," what are the</p> <p>12 two statements?</p> <p>13 BY MR. HUGHES:</p> <p>14 Q We asked you two questions about</p> <p>15 specific points of discussions with your</p> <p>16 colleagues at VCU and if you could point to</p> <p>17 specific discussions with them.</p> <p>18 A I think you've asked me multiple</p> <p>19 questions about my discussions with colleagues at</p> <p>20 VCU.</p> <p>21 Q I asked you a question, you -- you</p> <p>22 cannot point to any specific discussions with a</p>	<p style="text-align: right;">Page 277</p> <p>1 aiming at the treatment site and holding the</p> <p>2 device nozzle approximately 2 to 4 centimeters,</p> <p>3 apply even pressure at the center of the syringe</p> <p>4 to dispense the mixed solution. 21, Continue</p> <p>5 applying the sealant until a thin coating -- 1 to</p> <p>6 2 millimeters approximately -- is formed. Note</p> <p>7 about gauging thickness, Ensure that all suture</p> <p>8 knots are completely covered with hyd- -- et</p> <p>9 cetera.</p> <p>10 That -- that's discussing the same</p> <p>11 topic. This is an observable change that occurs</p> <p>12 with application.</p> <p>13 Q And this discusses a correlation</p> <p>14 between the observable change and a predetermined</p> <p>15 thickness?</p> <p>16 A Yes, it does. I believe it does.</p> <p>17 Q So other than citations to the IFUs and</p> <p>18 paragraph 35, 36, 37, 38 we've already</p> <p>19 discussed --</p> <p>20 A I would include 30- -- 31 and 32 as</p> <p>21 well. The portions -- the portions of 31 that we</p> <p>22 just read, and then in paragraph 32, again, the</p>

<p style="text-align: right;">Page 278</p> <p>1 last portion of the excerpted IFU. It's, you 2 know, minimally different than paragraph 31 but 3 again discusses that topic. 4 So back to your original question was 5 there other portions, and I -- I don't -- I can't 6 say no. I think these apply to what -- the topic 7 we're discussing. 8 Paragraph 28 I think I'd also include 9 the last -- last sentence: My opinion with 10 respect to these claims is that the selected 11 concentration of visualization agent in the -- I'm 12 skipping the parenthesis -- in the accused Adherus 13 product causes a visibly observable change 14 indicating a predetermined thickness. 15 Also related. 16 Q For the understanding of what a 17 correlation is between an observable change and a 18 predetermined thickness, are you relying upon your 19 own understanding of what a correlation would be 20 construed as or are you relying upon the 21 understanding provided to you from some other 22 source?</p>	<p style="text-align: right;">Page 280</p> <p>1 technical feature I'm able to comment on without 2 relying on Dr. Hays -- Dr. Mays. 3 BY MR. HUGHES: 4 Q So the correlation you can opine upon 5 independently apart from your discussions with 6 Dr. Mays? 7 A There -- yes, with the caveat that 8 there may be -- in some of the claims related to 9 observable change, there may be a chemical term in 10 that claim language that I would rely on him -- 11 Q Okay. 12 A -- to assure me that it -- it met the 13 definition that I understood it. 14 Q Let's talk briefly about your -- more 15 generally about your discussions with Dr. Mays. 16 In paragraph 15 -- it comes over to 17 page 6, the last bullet point -- you identify a 18 conversation with Dr. Jimmy Mays. 19 Do you see that? 20 A I'm on page 6, paragraph 15, last 21 bullet? 22 Q Yes.</p>
<p style="text-align: right;">Page 279</p> <p>1 A To define "correlation," this is the 2 correlation between the color change and the 3 predetermined thickness? 4 Q Between an observable change and a 5 predetermined thickness. 6 A Okay. I would use observable -- okay. 7 Between the observable -- the correlation between 8 the observable change and the predetermined 9 thickness, am I relying on my own opinions? Yes. 10 Am I relying on the -- for example, the court's 11 definitions? Yes, I am. 12 Q But for what meets the correlation -- 13 how correlation is construed, are you relying upon 14 Dr. Mays informing you of where a correlation is 15 or relying upon your own independent analysis? 16 MR. ALTHERR: Object to the form. 17 THE WITNESS: If we went through the 18 claims, there may be elements of some of the 19 claims that relate to correlation that involve 20 chemical terms that I discussed with Dr. Hays 21 [sic] and relied on him. But for the most part, 22 the correlation is not something -- that's a</p>	<p style="text-align: right;">Page 281</p> <p>1 A I'm there. Yes, sir. 2 Q And is this addressing a single 3 conversation or more than one conversation? 4 A He -- a single conversation with 5 Dr. Mays. 6 Q In preparation of this report, did you 7 have more than one conversation with Dr. Mays? 8 A I believe -- I can recall one 9 conversation distinctly, so I believe only one 10 conversation. 11 Q And that was a verbal conversation; no 12 email back and forth? 13 A That is my recollection, yes. 14 Q And how long did this conversation 15 last? 16 A I would estimate an hour. 17 Q All right. When was this conversation? 18 A July of 2017. 19 Q Did you have any conversations with 20 anyone regarding your opinions expressed in this 21 report other than what's listed in paragraph 15? 22 I'll exclude your counsel if your</p>

<p style="text-align: right;">Page 282</p> <p>1 (unintelligible) of course.</p> <p>2 MR. ALTHERR: Would you read the</p> <p>3 question back, please?</p> <p>4 (The Record was read as requested.)</p> <p>5 MR. ALTHERR: Object to the form.</p> <p>6 THE WITNESS: (Reviews document.)</p> <p>7 No.</p> <p>8 BY MR. HUGHES:</p> <p>9 Q In your conversation with Dr. Mays, did</p> <p>10 he provide you with any specific claim</p> <p>11 construction interpretations?</p> <p>12 A I guess it depends on how you define</p> <p>13 claim construction interpretations. My ability to</p> <p>14 interpret some of the claims is absolutely</p> <p>15 dependent on his explanations of those terms.</p> <p>16 Yes, he did provide that for me. And, hence, my</p> <p>17 understanding of the chemical specifics as things</p> <p>18 that are outside my expertise.</p> <p>19 Q Where in your report do you identify</p> <p>20 the specific claim terms that Dr. Mays helped you</p> <p>21 form the opinion on?</p> <p>22 A (Witness reviews document.)</p>	<p style="text-align: right;">Page 284</p> <p>1 the term.</p> <p>2 MR. ALTHERR: Object to the form.</p> <p>3 THE WITNESS: I may have relied on -- I</p> <p>4 certainly relied on both of those, but in the case</p> <p>5 of molecular weight since that's what you're</p> <p>6 specifically asking, this is also covered in the</p> <p>7 August report from Judge Burke.</p> <p>8 BY MR. HUGHES:</p> <p>9 Q Other than reactive precursor species</p> <p>10 comprising electrophilic functional groups, are</p> <p>11 there other express claim terms that you relied</p> <p>12 upon Dr. Mays for, for a construction, that were</p> <p>13 not included in the court's constructions?</p> <p>14 A I suspect there were, yes.</p> <p>15 Q Do you know approximately how many</p> <p>16 terms?</p> <p>17 A No, I don't. Not thousands. I would</p> <p>18 guess under a hundred such terms.</p> <p>19 Q So in an hour conversation, you</p> <p>20 discussed under a hundred such terms with</p> <p>21 Dr. Mays?</p> <p>22 A I think that's an accurate</p>
<p style="text-align: right;">Page 283</p> <p>1 Where I talk about that is in</p> <p>2 paragraph 19, specifically the later part on</p> <p>3 page 9, which we've gone through a little bit</p> <p>4 previously, where I give examples of some of the</p> <p>5 technical features that we discussed that he would</p> <p>6 help me with.</p> <p>7 Q And reactive precursor species</p> <p>8 comprise -- comprising electrophilic functional</p> <p>9 groups, is that one of them?</p> <p>10 A Yes, it is.</p> <p>11 Q And is, quote, molecular weight one of</p> <p>12 them?</p> <p>13 A I think it -- molecular weight, while</p> <p>14 it came up in our discussion, is probably not</p> <p>15 something he had to help me as much understand;</p> <p>16 although, it is listed as something that Judge</p> <p>17 Burke specifically listed, and I read that.</p> <p>18 Q Maybe I should rephrase the question</p> <p>19 slightly.</p> <p>20 Instead of help you understand, that</p> <p>21 you're relying upon his provided construction of</p> <p>22 what the term is versus your own construction of</p>	<p style="text-align: right;">Page 285</p> <p>1 approximation.</p> <p>2 Q And you also discussed his reports</p> <p>3 underlying the infringement contentions in that</p> <p>4 hour conversation?</p> <p>5 A Correct.</p> <p>6 Q What else did you discuss in that hour</p> <p>7 conversation?</p> <p>8 A We went through the patent claims in</p> <p>9 detail. We discussed polymers. I mean --</p> <p>10 Q Can you identify any -- anywhere in</p> <p>11 your report where there's a claim term that you're</p> <p>12 relying upon Dr. Mays for its construction?</p> <p>13 A Now that I've looked, would you mind</p> <p>14 rereading it?</p> <p>15 Q Can you identify anywhere in your</p> <p>16 report where there's a claim term that you're</p> <p>17 relying upon Dr. Mays for its construction?</p> <p>18 A I don't see others listed. There</p> <p>19 are -- other than I notice on page 9, there are</p> <p>20 two other excerpted portions from Judge Burke's</p> <p>21 report which mention macromolecule -- the first</p> <p>22 one mentions macromolecule, small molecule. The</p>

<p style="text-align: right;">Page 286</p> <p>1 second one mentions crosslinks. And these are</p> <p>2 things, for example -- although commented on in</p> <p>3 the judge's report -- that we discussed, and I</p> <p>4 certainly relied on his explanations.</p> <p>5 Q Are there any other terms you can</p> <p>6 identify in the report?</p> <p>7 A I don't see others in the report that I</p> <p>8 can explicitly remember discussing or relying on</p> <p>9 his . . .</p> <p>10 Q Can you turn to page -- paragraph 26 --</p> <p>11 pardon me, 27?</p> <p>12 A Okay. I'm on 27.</p> <p>13 Q Is it your opinion that the DuraSeal</p> <p>14 product practices the asserted patents?</p> <p>15 A Yes.</p> <p>16 Q Is it your opinion that the DuraSeal</p> <p>17 product practices every asserted claim you opine</p> <p>18 in your report that the Adherus product infringes?</p> <p>19 MR. ALTHERR: Could you read that back,</p> <p>20 please?</p> <p>21 (The Record was read as requested.)</p> <p>22 THE WITNESS: Yes.</p>	<p style="text-align: right;">Page 288</p> <p>1 that meets the asserted claim limitations is 1 to</p> <p>2 2 millimeters?</p> <p>3 MR. ALTHERR: Object to the form.</p> <p>4 THE WITNESS: Among a wider range, yes,</p> <p>5 if we pull a specific -- I believe the range for</p> <p>6 DuraSeal, actually, is wider and encompasses 1 to</p> <p>7 2 millimeters.</p> <p>8 BY MR. HUGHES:</p> <p>9 Q Okay.</p> <p>10 A So it overlaps with that range, yes.</p> <p>11 Q And earlier in that paragraph, you --</p> <p>12 there's a sentence that says, IFU review and</p> <p>13 obstruction in these products are critically</p> <p>14 important to understanding how the product works</p> <p>15 before using it in an actual surgical setting to</p> <p>16 seal a durotomy.</p> <p>17 Do you see that?</p> <p>18 A Yes.</p> <p>19 Q And do you always follow the IFUs in</p> <p>20 surgical settings?</p> <p>21 A Yes, with very rare exceptions.</p> <p>22 Q And one exception would be using a</p>
<p style="text-align: right;">Page 287</p> <p>1 BY MR. HUGHES:</p> <p>2 Q And in paragraph 27, five lines down,</p> <p>3 do you see the line that says, The appropriate</p> <p>4 thickness of the coating specified by DuraSeal</p> <p>5 product IFU is 1 to 2 millimeters?</p> <p>6 A Yes, I do.</p> <p>7 Q Is it your opinion that the infringing</p> <p>8 predetermined thickness -- pardon me. Strike</p> <p>9 that.</p> <p>10 Is it your opinion that the</p> <p>11 predetermined thickness of the DuraSeal product</p> <p>12 that meets the asserted claim limitations is 1 to</p> <p>13 2 millimeters?</p> <p>14 MR. ALTHERR: Object to the form.</p> <p>15 THE WITNESS: Repeat it, please.</p> <p>16 THE COURT REPORTER: "Is it" --</p> <p>17 Do you want me --</p> <p>18 MR. HUGHES: I can do it.</p> <p>19 THE COURT REPORTER: Okay.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q Is it your opinion that the</p> <p>22 predetermined thickness of the DuraSeal product</p>	<p style="text-align: right;">Page 289</p> <p>1 product off-label; correct?</p> <p>2 A That's a good example of one.</p> <p>3 Q Is it your understanding that other</p> <p>4 surgeons may also use products off-label, also?</p> <p>5 A Yes.</p> <p>6 Q So then other surgeons may not follow</p> <p>7 the IFUs; correct?</p> <p>8 MR. ALTHERR: Object to the form.</p> <p>9 THE WITNESS: Absolutely.</p> <p>10 BY MR. HUGHES:</p> <p>11 Q Paragraph 28, if you look at the last</p> <p>12 sentence --</p> <p>13 A Okay.</p> <p>14 Q -- in the very last line, your --</p> <p>15 paragraph 8 appears at the beginning -- step back.</p> <p>16 Paragraph 28 at the beginning says,</p> <p>17 It's my opinion that a neurosurgeon or spinal</p> <p>18 surgeon using either DuraSeal or DuraSeal Xact in</p> <p>19 accordance with, and it continues.</p> <p>20 A Uh-huh.</p> <p>21 Q So it appears that 28 is addressing</p> <p>22 DuraSeal meeting the claim limitations of the</p>

<p style="text-align: right;">Page 290</p> <p>1 asserted claims; is that accurate?</p> <p>2 A I agree.</p> <p>3 Q And then if you move to the very last</p> <p>4 sentence, My opinion with respect to the claims is</p> <p>5 that the selected concentration, and it continues.</p> <p>6 Do you see that?</p> <p>7 A Yes, I do.</p> <p>8 Q In the last line it says, Adherus</p> <p>9 products cause a visually observable change.</p> <p>10 Are you opining about the Adherus</p> <p>11 products here or about the DuraSeal products?</p> <p>12 A Both.</p> <p>13 Q So this opinion is addressed to</p> <p>14 DuraSeal and Adherus products?</p> <p>15 A Yes.</p> <p>16 Q And you meant to opine on the Adherus</p> <p>17 products in paragraph 28?</p> <p>18 A I meant to opine on both products in</p> <p>19 paragraph 28.</p> <p>20 Q Let's look at paragraph 36. If you can</p> <p>21 compare the last sentence in paragraph 28 and</p> <p>22 paragraph 36.</p>	<p style="text-align: right;">Page 292</p> <p>1 said are there other typographical errors.</p> <p>2 Did I understand those?</p> <p>3 BY MR. HUGHES:</p> <p>4 Q We can read it back, but you're</p> <p>5 actually -- so --</p> <p>6 A I said it's possible that those two</p> <p>7 sentences are a typographical error, and you asked</p> <p>8 are there others, which implies that it was a</p> <p>9 typographical error. I just want to clarify it --</p> <p>10 it may be.</p> <p>11 Q In paragraph 28, is there any</p> <p>12 difference to the import of your opinion if you</p> <p>13 used the word "DuraSeal" versus "Adherus" in the</p> <p>14 last line?</p> <p>15 A No, that's a great point. They're</p> <p>16 interchangeable.</p> <p>17 Q They're interchangeable for your</p> <p>18 opinion provided in paragraph 28?</p> <p>19 A Correct. The substance of the sentence</p> <p>20 if you change that word doesn't change, in my</p> <p>21 opinion.</p> <p>22 I could compare them, but it may be</p>
<p style="text-align: right;">Page 291</p> <p>1 A Twenty-eight and 36, right here.</p> <p>2 Q Yeah. There's two paragraphs.</p> <p>3 A Okay.</p> <p>4 Q Look at the last sentence.</p> <p>5 A Yes.</p> <p>6 Q And compare the two last sentences.</p> <p>7 A Uh-huh.</p> <p>8 Q Is it possible that the referenced</p> <p>9 Adherus product in paragraph 28 was a</p> <p>10 typographical error?</p> <p>11 A Certainly that's possible.</p> <p>12 Q Do you have any other typographical</p> <p>13 errors in the -- your report you're aware of?</p> <p>14 MR. ALTHERR: Object to the form.</p> <p>15 THE WITNESS: Not that I'm aware of.</p> <p>16 And I would -- I don't think I -- the</p> <p>17 question you just asked me is am I aware of other</p> <p>18 typographical errors, and the sound of that</p> <p>19 question makes it -- the prior question you asked</p> <p>20 "is it possible." I said it's possible that it's</p> <p>21 a typographical error. I didn't say it was a</p> <p>22 typographical error. The following question you</p>	<p style="text-align: right;">Page 293</p> <p>1 word for word.</p> <p>2 (Witness reviews document.)</p> <p>3 Yeah.</p> <p>4 Q I don't think it's that important</p> <p>5 unless you feel a need to.</p> <p>6 A No, no, I said I could.</p> <p>7 Q Paragraph 35, if you could look at that</p> <p>8 for a minute.</p> <p>9 A Yes.</p> <p>10 Q You state here -- there's a sentence,</p> <p>11 My own observations of the HyperBranch videos</p> <p>12 demonstrate the user understands, and it</p> <p>13 continues.</p> <p>14 Do you see that sentence?</p> <p>15 A Yes.</p> <p>16 Q And you state, The user understands to</p> <p>17 stop applying the Adherus product at the point</p> <p>18 when there's a uniform, even coating changing the</p> <p>19 color of the target site.</p> <p>20 Do you see that?</p> <p>21 A Yes.</p> <p>22 Q What do you mean by "uniform, even</p>

<p style="text-align: right;">Page 294</p> <p>1 coating"?</p> <p>2 A So in the video -- in the initial</p> <p>3 portions of the video, which we're not looking at</p> <p>4 right now, the initial application you can see</p> <p>5 only a very faint amount of green color with no</p> <p>6 measurable obscuration of the underlying tissue</p> <p>7 planes, and some of them have none -- some</p> <p>8 portions of the incision have no coverage.</p> <p>9 And as the video progresses, you can</p> <p>10 see that the distribution and the application is</p> <p>11 more uniform across the suture line and completely</p> <p>12 covers and obscures the detail underneath it by</p> <p>13 the end of it -- progressively provides more color</p> <p>14 to that site.</p> <p>15 Q What does uniform mean to you in that</p> <p>16 context?</p> <p>17 A It means that the length of the</p> <p>18 incision is covered or obscured or its appearance</p> <p>19 has changed to a uniform amount or in a uniform</p> <p>20 amount.</p> <p>21 Q What is a uniform amount?</p> <p>22 A A similar amount, a degree of</p>	<p style="text-align: right;">Page 296</p> <p>1 Q So this opinion expressed here that the</p> <p>2 user understands to stop applying the Adherus</p> <p>3 product at the point when there's a uniform, even</p> <p>4 coating changing the color of the target side from</p> <p>5 the natural tissue color to an even green color.</p> <p>6 At this point the coating obscures the sutures,</p> <p>7 subjacent tissue plane or microvascular,</p> <p>8 indicating the user has reached a predetermined</p> <p>9 thickness of 1 or 2 millimeters specified in the</p> <p>10 Adherus product -- I understand it's a little more</p> <p>11 broad than what I just asked, but did you discuss</p> <p>12 this sentence and its import with Dr. Mays?</p> <p>13 A It is possible we discussed it, but I</p> <p>14 don't think Dr. Mays -- inclusive of that whole</p> <p>15 sentence, I don't think he influenced my opinion</p> <p>16 on that subject.</p> <p>17 Q So you're not relying upon Dr. Mays for</p> <p>18 your opinion in that sentence?</p> <p>19 A I agree with that rephrasing.</p> <p>20 Q Do you know whether Dr. Mays is relying</p> <p>21 upon your opinion provided in that sentence?</p> <p>22 A I can't speak for Dr. Mays.</p>
<p style="text-align: right;">Page 295</p> <p>1 obscuration that's the same.</p> <p>2 Q And when you say "the same," the same</p> <p>3 compared to what?</p> <p>4 A Compared to prior in the application</p> <p>5 where there was clear asymmetry in portions of the</p> <p>6 application site.</p> <p>7 Q And you said "asymmetry"; correct?</p> <p>8 A Correct, asymmetry. Lack of symmetry.</p> <p>9 Q And is there a difference between the</p> <p>10 meaning of "even" and "uniform" there?</p> <p>11 A No, I don't think there's a substantial</p> <p>12 difference between those two words.</p> <p>13 Q Is your opinion of what an even,</p> <p>14 uniform coating is, is that either an independent</p> <p>15 opinion or did you form that after talking with</p> <p>16 Dr. Mays?</p> <p>17 A I don't think my conversation with</p> <p>18 Dr. Mays informed my opinion on that subject.</p> <p>19 Q Did you and Dr. Mays discuss what an</p> <p>20 even, uniform green coating is?</p> <p>21 A No, I don't recall discussing that with</p> <p>22 Dr. Mays.</p>	<p style="text-align: right;">Page 297</p> <p>1 Q And when we were addressing, looking at</p> <p>2 paragraph 37 and 38, the bullet points with the</p> <p>3 IFU points and were saying the observable green</p> <p>4 color in the color change --</p> <p>5 Do you remember that discussion?</p> <p>6 A Yes.</p> <p>7 Q -- are those opinions opinions you</p> <p>8 formed independently or did you rely upon Dr. Mays</p> <p>9 for those opinions?</p> <p>10 A Without making -- without going back to</p> <p>11 that other conversation, the -- if we -- if we can</p> <p>12 avoid that, the opinions in those two paragraphs,</p> <p>13 37 and 38, to the degree they don't involve</p> <p>14 chemical terms, I also do not think that if I had</p> <p>15 any conversations with Dr. Mays -- and it's</p> <p>16 possible we talked about the application and the</p> <p>17 green color change -- I don't think it influenced</p> <p>18 my opinion or I don't think it led to my</p> <p>19 conclusions expressed in these two paragraphs, if</p> <p>20 that answers your questions.</p> <p>21 Q So it's fair to say you did not rely</p> <p>22 upon Dr. Mays' instructions to you in forming the</p>

<p style="text-align: right;">Page 298</p> <p>1 opinions in paragraphs 37 and 38?</p> <p>2 A The -- the -- the -- that's -- that's</p> <p>3 correct. I mean, the understanding of the --</p> <p>4 prior to being able to form these opinions, I had</p> <p>5 to be satisfied regarding the chemistry, the other</p> <p>6 things we discussed, so some base of an</p> <p>7 understanding regarding the hydrogel, certainly.</p> <p>8 But the conclusion in these paragraphs</p> <p>9 and the one we just discussed, I would agree</p> <p>10 they're not things that involve polymer chemistry</p> <p>11 and other topics that I relied on his expertise to</p> <p>12 form my own opinion.</p> <p>13 Q And your opinion of a color change of</p> <p>14 the hydrogel itself, you do not rely upon Dr. Mays</p> <p>15 for forming your opinion of a color change of the</p> <p>16 hydrogel itself; is that correct?</p> <p>17 A That is correct. I would agree with</p> <p>18 that.</p> <p>19 Q And for what a correlation is between</p> <p>20 an observable change and a predetermined</p> <p>21 thickness, is it accurate to say you did not rely</p> <p>22 upon Dr. Mays for that opinion?</p>	<p style="text-align: right;">Page 300</p> <p>1 been discussing, if you can turn to paragraph 27.</p> <p>2 A Twenty-seven.</p> <p>3 Q The portion on page 14.</p> <p>4 We talked about this briefly before;</p> <p>5 that you state here the appropriate thickness of</p> <p>6 the DuraSeal product is 1 to 2 millimeters?</p> <p>7 A Yes.</p> <p>8 Q Have you ever measured the thickness of</p> <p>9 a DuraSeal after you've applied it to a patient?</p> <p>10 A Yes.</p> <p>11 Q How have you measured the thickness of</p> <p>12 the DuraSeal product after you've applied it to a</p> <p>13 patient?</p> <p>14 A There's a ruler in every surgical set.</p> <p>15 It has millimeters on it. And we use the ruler.</p> <p>16 Q And is that the standard practice that</p> <p>17 you use when applying DuraSeal -- to measure its</p> <p>18 thickness?</p> <p>19 A No, I wouldn't say it's standard.</p> <p>20 Q How often do you measure the thickness</p> <p>21 of the DuraSeal product once you've applied it?</p> <p>22 A It's hard to estimate an exact</p>
<p style="text-align: right;">Page 299</p> <p>1 A I think that's accurate, yes.</p> <p>2 MR. HUGHES: I'm at a stopping point.</p> <p>3 We've been going a little bit. If the witness</p> <p>4 would like to break, we can break, or I can move</p> <p>5 to the next --</p> <p>6 MR. ALTHERR: Take about five minutes?</p> <p>7 MR. HUGHES: Yeah.</p> <p>8 THE WITNESS: Sure. Let's take a</p> <p>9 quick -- is that all right?</p> <p>10 MR. HUGHES: Yeah, yeah.</p> <p>11 THE VIDEOGRAPHER: This concludes disk</p> <p>12 number 3 of the video deposition of Dennis Rivet,</p> <p>13 M.D. The time is 2:57:26 p.m. We're now off the</p> <p>14 record.</p> <p>15 (Recess -- 2:57 p.m.)</p> <p>16 (After recess -- 3:07 p.m.)</p> <p>17 THE VIDEOGRAPHER: This begins disk</p> <p>18 number 4 of the video deposition of Dennis Rivet,</p> <p>19 M.D. The time is 3:07:14 p.m.</p> <p>20 We are now on the record.</p> <p>21 BY MR. HUGHES:</p> <p>22 Q Dr. Rivet, in your opening report we've</p>	<p style="text-align: right;">Page 301</p> <p>1 percentage of time. Not usually, less than a</p> <p>2 quarter of the time. 10 percent, 20 percent of</p> <p>3 the time if you have . . .</p> <p>4 Q Why would you measure the thickness of</p> <p>5 the DuraSeal product after you've applied it?</p> <p>6 A It's nice to get some feedback</p> <p>7 regarding if you -- sometimes you -- you can</p> <p>8 dislodge it accidentally; sometimes you decide to</p> <p>9 reclose it. And particularly in spinal cases,</p> <p>10 there's a concern that you don't want to -- you</p> <p>11 want to limit the amount you're putting, and it's</p> <p>12 nice to quantify that sometimes, have an idea of</p> <p>13 what was in place.</p> <p>14 Q And is it your opinion that other</p> <p>15 neurosurgeons measure the thickness of the</p> <p>16 DuraSeal product after they apply it?</p> <p>17 A I'm sure they do, yes. I'm sure it's</p> <p>18 done by other spinal surgeons and neurosurgeons.</p> <p>19 Q We were discussing in relation to</p> <p>20 paragraph 35 earlier today your discussions with</p> <p>21 other colleagues at VCU.</p> <p>22 Do you remember that discussion?</p>

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1 A Yes.

2 Q Are you -- for your opinions in this

3 report, are you relying upon any of their

4 statements about them measuring the thickness of

5 the Adherus product that they applied?

6 A No.

7 Q Are you aware of anyone at VCU

8 measuring the thickness of the Adherus product

9 after it was applied?

10 A No.

11 Q In the opinion provided in your opening

12 report, are you relying upon an example of any --

13 anyone ever measuring the thickness of the Adherus

14 product once it was applied?

15 A No.

16 (Deposition Exhibit 412 was marked for

17 identification and attached to the transcript.)

18 BY MR. HUGHES:

19 Q Dr. Rivet, the court reporter has

20 handed you what's been marked as Exhibit 412.

21 Do you recognize this document?

22 A Yes, this is the rebuttal expert

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1 report.

2 Q If you flip to the last page, page 22,

3 is it dated October 2nd, 2017?

4 A Yes, it is.

5 Q And is that your signature?

6 A Yes, it is.

7 Q And as of October 2nd, 2017, is this a

8 complete statement of all opinions expressed in

9 the report and the basis and reasons for those

10 opinions?

11 MR. ALTHERR: Object to form.

12 THE WITNESS: Yes.

13 BY MR. HUGHES:

14 Q And as of October 2nd, 2017, does this

15 report contain all the facts or data considered in

16 forming your opinions?

17 MR. ALTHERR: Object to the form.

18 THE WITNESS: I believe it does, yes.

19 BY MR. HUGHES:

20 Q And as of October 17th, 2000 -- strike

21 that.

22 As of October 2nd, 2017, does this

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1 report contain any exhibits that you'll -- be used

2 to summarize or support your opinions?

3 A Does that include, for example, videos

4 as an exhibit? Could you define "exhibits"?

5 Q Sure.

6 So apart from the videos which clearly

7 are not in the report -- you identify it -- but

8 does it identify any other exhibits you might use

9 to summarize or support your opinions?

10 A Could you define "exhibits" -- a

11 potential -- what might be a potential exhibit?

12 Q A graph or a diagram or some other

13 demonstrative of your opinions.

14 A That are not in the report?

15 Q Yeah.

16 The question is does the report contain

17 any exhibit that would be used to summarize or

18 support your opinions?

19 MR. ALTHERR: Object to the form.

20 THE WITNESS: So there are some

21 articles, I believe, that are contained within the

22 report. Are those --

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1 BY MR. HUGHES:

2 Q Well, they're contained as exhibits to

3 the report; correct?

4 A They are.

5 Q So the word "exhibit" might be a little

6 confused there. But the exhibits to the report

7 I'm treating as being contained in the report.

8 A Okay. I'm sorry. I'm not

9 understanding the question or --

10 Q Does the report that you've been handed

11 here and is in your hand --

12 A Yes.

13 Q -- contain all of the exhibits that may

14 be used to summarize or support your -- your

15 report --

16 MR. ALTHERR: Object to --

17 BY MR. HUGHES:

18 Q -- other than --

19 MR. ALTHERR: -- the form.

20 BY MR. HUGHES:

21 Q -- the videos we discussed, of course?

22 MR. ALTHERR: Object to the form.

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1 THE WITNESS: I believe it does, yes.
 2 BY MR. HUGHES:
 3 Q And you identify in paragraph 2 that
 4 your CV had not changed since the beginning of
 5 your opening report; is that accurate?
 6 A I would have to review the CV with
 7 my ...
 8 Q If you look at paragraph 2 of your
 9 rebuttal report --
 10 A Okay.
 11 Q -- it says since the time you have not
 12 testified or been deposed, has not changed
 13 [verbatim]. And I -- the compensation has not
 14 changed.
 15 Had your CV significantly changed
 16 between --
 17 A Did you say "significantly changed"?
 18 Q Yes.
 19 A No, it has not significantly changed.
 20 Q And did it -- has it changed in any way
 21 that would affect your opinions in this report?
 22 A No.

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1 Q And had your opinions changed -- the
 2 opinions expressed in your opening report on
 3 September 8th, 2017, had any of those opinions
 4 changed between then and October 2nd, 2017, when
 5 you filed your rebuttal report?
 6 A I can't think of any substantial
 7 opinion changes between those two.
 8 Q And earlier we were discussing the
 9 deposition testimony of other surgeons that has
 10 been given in this case.
 11 Do you remember that discussion?
 12 A Yes.
 13 Q And you mentioned you first learned
 14 that other surgeons in this case had been -- had
 15 given deposition testimony when you were reading
 16 the rebuttal report.
 17 A (Witness nods head.)
 18 Q Which rebuttal report were you reading?
 19 A My recollection, it was Dr. Flombaum.
 20 Am I pronouncing that correctly?
 21 Q I think so, yes.
 22 And after you were made aware of the

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1 surgeon testimony in this case, did you review
 2 that surgeon testimony?
 3 A I did.
 4 Q Did you review that surgeon testimony
 5 in full?
 6 A I believe I did.
 7 Q And there are nine surgeons that gave
 8 testimony; does that seem accurate to you?
 9 A I believe I may have reviewed more,
 10 but, yes, that's roughly accurate.
 11 Q Okay. And did you contemplate filing a
 12 reply report in this case?
 13 A I knew it was an option, yes.
 14 Q Did you file a reply report in this
 15 case?
 16 A No.
 17 Q And after reviewing the surgeon
 18 testimony of -- that you reviewed, you still chose
 19 not to file a reply report?
 20 A Correct.
 21 Q Did you review -- of the surgeon
 22 testimony you reviewed, did you review the full

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1 testimony of those surgeons?
 2 A I believe I did, yes.
 3 Q And you still chose not to file a reply
 4 report?
 5 A Correct.
 6 Q So there wasn't anything in that
 7 surgeon testimony that prompted you to want to
 8 file the reply report?
 9 A That's correct.
 10 Q So you don't believe anything in that
 11 surgeon testimony contradicts the opinions you set
 12 forth in your initial opening expert report?
 13 A No, I think one -- there are -- there
 14 are statements in some of those testimonies that
 15 are not in agreement with my opinion. I think one
 16 could easily read some of the details, and I
 17 wouldn't agree with them or they could sound
 18 different.
 19 But I wouldn't agree with your
 20 statement.
 21 Q But even though you -- you identified
 22 potentially some inconsistencies with your

<p style="text-align: right;">Page 310</p> <p>1 opinions, you knew you had the option to file a</p> <p>2 reply report but you chose not to file a reply</p> <p>3 report -- reply report; is that accurate?</p> <p>4 A Yes, it is.</p> <p>5 Q Why didn't you file a reply report?</p> <p>6 A Because the -- to use your word, the</p> <p>7 inconsistencies were not of substance that I felt</p> <p>8 it was important.</p> <p>9 Q If you can turn to paragraph 7 in your</p> <p>10 rebuttal report. That's Exhibit 412.</p> <p>11 A Paragraph 7, I'm there.</p> <p>12 Q And you mention you viewed videos</p> <p>13 showing hydrogel containing barium sulfate.</p> <p>14 Are all those videos -- strike that.</p> <p>15 Are all the videos you identified and</p> <p>16 relied upon in this report identified in the</p> <p>17 report -- strike that.</p> <p>18 Are all the videos you relied upon in</p> <p>19 forming your opinions in this rebuttal report</p> <p>20 identified in the report?</p> <p>21 A Yes, I believe they are.</p> <p>22 Q And you say, I understand the videos</p>	<p style="text-align: right;">Page 312</p> <p>1 anything about these experiments with Dr. Mays</p> <p>2 prior to him discussing -- prior to him conducting</p> <p>3 the experiments?</p> <p>4 MR. ALTHERR: Objection to form.</p> <p>5 THE WITNESS: Not that I recall.</p> <p>6 BY MR. HUGHES:</p> <p>7 Q In paragraph 8 you say, The materials I</p> <p>8 reviewed and considered with respect to this</p> <p>9 rebuttal report are expressly identified</p> <p>10 throughout the body of this report.</p> <p>11 Do you see that?</p> <p>12 A Yes.</p> <p>13 Q Is there anything in -- that you relied</p> <p>14 upon in forming your opinions in this rebuttal</p> <p>15 report that have not been identified in this</p> <p>16 report?</p> <p>17 A I believe that's similar to -- no, I</p> <p>18 don't know of anything that I've failed to</p> <p>19 identify.</p> <p>20 Q In forming your opinions of this</p> <p>21 rebuttal report, did you rely upon your</p> <p>22 conversations with your colleagues at VCU that</p>
<p style="text-align: right;">Page 311</p> <p>1 are experiments conducted by or at the direction</p> <p>2 of Dr. Mays.</p> <p>3 Do you see that?</p> <p>4 A Yes.</p> <p>5 Q Were you present during any of these</p> <p>6 experiments?</p> <p>7 A No.</p> <p>8 Q Did you help direct or facilitate any</p> <p>9 of these experiments?</p> <p>10 A No.</p> <p>11 Q Were you involved in any way in any of</p> <p>12 these experiments?</p> <p>13 A No.</p> <p>14 Q Is it fair to say that you saw -- you</p> <p>15 just saw the results of the experiments from</p> <p>16 Dr. Mays?</p> <p>17 A That's fair to say.</p> <p>18 Q Did you have a conversation with</p> <p>19 Dr. Mays prior to him conducting these</p> <p>20 experiments?</p> <p>21 Strike that.</p> <p>22 Did you have a conversation regarding</p>	<p style="text-align: right;">Page 313</p> <p>1 were discussed in paragraph 35 of your opening</p> <p>2 report?</p> <p>3 A Yes. I think it would be impossible</p> <p>4 for me to separate my opinions from one report to</p> <p>5 the rebuttal what influenced -- it would be</p> <p>6 impossible for me to say, no, in no way did prior</p> <p>7 conversations that I had over a period of months</p> <p>8 with multiple individuals have no bearing on an</p> <p>9 opinion I expressed.</p> <p>10 So I would have to say, yes, they did</p> <p>11 in some way inform did.</p> <p>12 Q Do you identify those discussions with</p> <p>13 your colleagues at VCU anywhere in your rebuttal</p> <p>14 report?</p> <p>15 A I don't believe I do.</p> <p>16 Q And why did you not identify those</p> <p>17 discussions with your colleagues at VCU in your</p> <p>18 rebuttal report?</p> <p>19 MR. ALTHERR: Object to the form.</p> <p>20 THE WITNESS: They had already been</p> <p>21 identified in the previous report.</p> <p>22 BY MR. HUGHES:</p>

<p style="text-align: right;">Page 314</p> <p>1 Q So they were already identified in</p> <p>2 paragraph 35 of the previous report?</p> <p>3 A That's correct.</p> <p>4 Q And it's your position -- strike that.</p> <p>5 So your opinion that -- and your</p> <p>6 reliance you formed upon those discussions to form</p> <p>7 your -- strike that.</p> <p>8 It's your opinion that your reliance</p> <p>9 upon those discussions with your colleagues at VCU</p> <p>10 that you relied upon to form your opinion in</p> <p>11 rebuttal report was sufficiently disclosed in</p> <p>12 paragraph 35 of your opening report?</p> <p>13 MR. ALTHERR: Object to form.</p> <p>14 BY MR. HUGHES:</p> <p>15 Q Is that accurate?</p> <p>16 A Yes.</p> <p>17 Q And for the same reasons we discussed</p> <p>18 earlier; that you believed that they were</p> <p>19 sufficiently disclosed in your opening report?</p> <p>20 A Yes.</p> <p>21 Q Any additional reasons why you feel</p> <p>22 they were sufficiently disclosed to support the</p>	<p style="text-align: right;">Page 316</p> <p>1 hydrogel applied at all in the video Adherus</p> <p>2 AutoSpray Following Temporal Lobectomy?</p> <p>3 A No.</p> <p>4 Q Did you measure the thickness of the</p> <p>5 hydrogel applied in the other video that you</p> <p>6 relied upon to form your opinions?</p> <p>7 A No.</p> <p>8 Q In forming your opinions today --</p> <p>9 strike that.</p> <p>10 In forming your opinions in your</p> <p>11 rebuttal report, did you rely upon any videos</p> <p>12 other than the barium sulfate videos we discussed</p> <p>13 earlier and the Adherus AutoSpray Following</p> <p>14 Temporal Lobectomy and the previous Adherus</p> <p>15 demonstration video we discussed?</p> <p>16 A I don't believe you didn't mention the</p> <p>17 fibular collagen video. But, yes --</p> <p>18 Q Okay.</p> <p>19 A -- those -- it included all four of</p> <p>20 those videos.</p> <p>21 Q Looking at paragraph 16, the first</p> <p>22 image, on page 6 --</p>
<p style="text-align: right;">Page 315</p> <p>1 opinions in your rebuttal report?</p> <p>2 A "They" refers to my conversations</p> <p>3 referenced in paragraph 35?</p> <p>4 Q Correct.</p> <p>5 A No additional reasons.</p> <p>6 Q Did you have additional conversations</p> <p>7 with your colleagues at VCU that you relied upon</p> <p>8 to form your opinions in your rebuttal report</p> <p>9 other than the ones we discussed this morning in</p> <p>10 context of your opening report?</p> <p>11 A No, not that I recall.</p> <p>12 Q If we can look at paragraph 16 of your</p> <p>13 rebuttal report. In paragraph 16, you show three</p> <p>14 images from a video; is that accurate?</p> <p>15 A Yes.</p> <p>16 Q And these are from the Adherus</p> <p>17 AutoSpray Following Temporal Lobectomy video?</p> <p>18 A Yes.</p> <p>19 Q And did you measure the thickness of</p> <p>20 the hydrogel applied in any of these images?</p> <p>21 A No.</p> <p>22 Q Did you measure the thickness of the</p>	<p style="text-align: right;">Page 317</p> <p>1 A Yes.</p> <p>2 Q -- do you have any objection --</p> <p>3 objective measurement of how thick the hydrogel is</p> <p>4 applied in that video -- in that photo?</p> <p>5 A I do not.</p> <p>6 Q And looking at the photo at the top of</p> <p>7 page 7, do you have any objective measurement of</p> <p>8 how thick the hydrogel is that's been applied in</p> <p>9 that photo?</p> <p>10 A I do not.</p> <p>11 Q And same question at the photo at the</p> <p>12 bottom of page 7. Do you have any objective</p> <p>13 measurement how thick the hydrogel is that has</p> <p>14 been applied in that photo?</p> <p>15 A The only objective -- the only</p> <p>16 objective measurement could be drawn from the fact</p> <p>17 that there's a human skull adjacent to the field.</p> <p>18 And certainly I know the range of thickness of a</p> <p>19 human skull anatomically, and one can objectively</p> <p>20 say it is less than the thickness of the skull.</p> <p>21 More specifically than that, no.</p> <p>22 Q So that's interesting.</p>

<p style="text-align: right;">Page 318</p> <p>1 So based on your experience as a</p> <p>2 neurosurgeon, you have -- is it fair to say you</p> <p>3 have a pretty good idea of the range of thickness</p> <p>4 that a human skull is?</p> <p>5 A Yes.</p> <p>6 Q And by looking at this photo on the</p> <p>7 bottom of page 7 and based upon your experience</p> <p>8 and knowledge of what the thickness of the human</p> <p>9 skull is, you can interpolate a rough idea of how</p> <p>10 thick the hydrogel is; is that accurate?</p> <p>11 A That's correct. I think one can say</p> <p>12 within this -- the limits of a two-dimensional</p> <p>13 video -- and this is a screen grab -- that the</p> <p>14 thickness of the product is less than the</p> <p>15 thickness of this patient's skull.</p> <p>16 Q Now, you've never used an Adherus</p> <p>17 product; correct?</p> <p>18 A That is correct.</p> <p>19 Q When you're applying -- but you have</p> <p>20 used the DuraSeal product; correct?</p> <p>21 A Yes.</p> <p>22 Q When you're applying the DuraSeal</p>	<p style="text-align: right;">Page 320</p> <p>1 Q And again in paragraph 16, the</p> <p>2 second -- pardon me, the third sentence, it says,</p> <p>3 There is not a uniform green color of the Adherus</p> <p>4 product that allows a user to gauge whether the</p> <p>5 predetermined thickness -- and it gives a range --</p> <p>6 has been applied.</p> <p>7 Do you see that?</p> <p>8 A I'm sorry. I had trouble finding that</p> <p>9 sentence. What page are you on --</p> <p>10 Q Yes.</p> <p>11 A -- 6 or 7?</p> <p>12 Q Paragraph 16, page 6.</p> <p>13 A Page 6, okay.</p> <p>14 Q Yeah, it gets confusing with the page</p> <p>15 numbers and the paragraph numbers.</p> <p>16 Paragraph 16, page 6, the third line</p> <p>17 down, it states, There is not a uniform green</p> <p>18 color of the Adherus product that allows the user</p> <p>19 to gauge whether the predetermined thickness, for</p> <p>20 example, 1 to 2 millimeters, has been applied.</p> <p>21 Do you see that?</p> <p>22 A Yes.</p>
<p style="text-align: right;">Page 319</p> <p>1 product, do you use information like that, like,</p> <p>2 for example, the thickness of the human skull or</p> <p>3 other indicia to help guide you -- your</p> <p>4 understanding of how thick the DuraSeal product is</p> <p>5 you've applied?</p> <p>6 A Yes, I think the application is</p> <p>7 informed by the anatomic landmarks of the surgical</p> <p>8 field. Yes.</p> <p>9 Q And when you're applying the DuraSeal</p> <p>10 product, you're observing all those anatomical</p> <p>11 landmarks of the surgical field at the same time</p> <p>12 that you're applying the product; correct?</p> <p>13 A The first line of your question, would</p> <p>14 you mind re- -- did you specifically ask about --</p> <p>15 Q When you're applying the DuraSeal --</p> <p>16 A Yes.</p> <p>17 Q -- product.</p> <p>18 A Yes.</p> <p>19 Q Do you have any reason to believe it</p> <p>20 would not be the same when a surgeon is applying</p> <p>21 an Adherus product?</p> <p>22 A I do not.</p>	<p style="text-align: right;">Page 321</p> <p>1 Q And in forming this opinion here, did</p> <p>2 you rely upon Dr. Mays for what you believe a</p> <p>3 uniform green color of the Adherus product</p> <p>4 entails?</p> <p>5 A No.</p> <p>6 Q And for the idea of "allows a user to</p> <p>7 gauge whether a predetermined thickness has been</p> <p>8 applied," that portion of your opinion, did you</p> <p>9 reply -- rely upon Dr. Mays' understanding for</p> <p>10 that opinion?</p> <p>11 A No.</p> <p>12 Q In looking at the -- the section that</p> <p>13 begins at paragraph 14, it's titled Rebuttal to</p> <p>14 Dr. Flombaum's Opinion --</p> <p>15 A Okay. I'm there.</p> <p>16 Q -- did you rely upon your discussion</p> <p>17 with Dr. Mays for your opinions in this section,</p> <p>18 which to be clear I believe is paragraphs 14</p> <p>19 through 19 -- pardon me, paragraph 18 of your</p> <p>20 report?</p> <p>21 A The question is did I rely on Dr. Mays</p> <p>22 for paragraphs 14 through 18 inclusive?</p>

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1 **Q Correct.**

2 A So you're expanding it now to include

3 all of those paragraphs?

4 **Q Well, I believe this is the section**

5 **under the heading Rebuttal to Dr. Flombaum's**

6 **Opinion.**

7 A Yes. And you're asking for this

8 section did I rely on Dr. Mays' opinions for any

9 portions of it?

10 **Q That's my question.**

11 A (Witness reviews document.)

12 I've looked through Sections 14 through

13 18, and my answer would be, no, these opinions

14 were -- did not rely on Dr. Mays with the caveat

15 that I gave you before, some of my understanding

16 of the polymer chemistry during our initial

17 discussion factored into my understanding of the

18 hydrogel.

19 But nothing specific in these 14, 15,

20 16, 17 and 18 paragraphs, I can identify that I

21 relied on Dr. Mays' opinion to form.

22 **Q After you submitted your first report**

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1 **in this litigation on September 2nd and before you**

2 **submitted your rebuttal report -- pardon me,**

3 **September 8th --**

4 A Just making sure.

5 **Q Yeah.**

6 **Strike that.**

7 **After you submitted your opening report**

8 **on September 8th, but before you submitted your**

9 **rebuttal report on October 2nd, in this**

10 **litigation, did you have any conversations with**

11 **Dr. Mays?**

12 A Not that I recall.

13 **Q So in preparing your rebuttal report in**

14 **this case, other than the one -- the single**

15 **one-hour conversation you had with Dr. Mays**

16 **previously, you had no other conversations with**

17 **Dr. Mays?**

18 A Approximately one hour. I believe

19 that's correct. I don't recall a discussion

20 between those two time points.

21 **Q Okay.**

22 A Specifically, September 8th to

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1 October 2nd.

2 **Q So you're not relying upon any new**

3 **conversations with Dr. Mays to form your opinions**

4 **in your October 2nd report?**

5 A That's an accurate statement I agree

6 with.

7 **Q Okay. Looking at paragraph 18 of your**

8 **rebuttal report --**

9 A I'm there.

10 **Q -- the fourth line down says, I**

11 **understand was raised by defendant that**

12 **correlation required, and the sentence goes on.**

13 A Uh-huh.

14 **Q Do you see that?**

15 A Yes.

16 **Q What was that understanding based upon?**

17 A I under- -- let me just read the full

18 sentence if I could, please.

19 (Witness reviews document.)

20 Dr. Flombaum's report.

21 **Q The fact that defendant -- the --**

22 **the -- your understanding that defendant had**

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1 **raised the correlation requirement required a**

2 **specific color at each particular thickness, that**

3 **was -- that's based upon Dr. Flom- -- strike that.**

4 **Your understanding that defendant**

5 **raised that a correlation required a particular**

6 **thickness -- pardon me. Strike that.**

7 **Your understanding that defendant**

8 **raised the question that a correlation required a**

9 **particular specific color at each particular**

10 **thickness, i.e., a particular RGB value for each**

11 **and every particular thickness, that's based on**

12 **Dr. Flombaum's report?**

13 A And the court --

14 MR. ALTHERR: Objection to the form.

15 THE WITNESS: Sorry. Excuse me.

16 And the court's construction. The

17 first sentence of that paragraph lists both, and I

18 agree with that.

19 BY MR. HUGHES:

20 **Q Were you provided with defendant's**

21 **briefing in the claim construction phase of this**

22 **case to read an analysis of your -- in preparation**

<p style="text-align: right;">Page 326</p> <p>1 of your report?</p> <p>2 A I don't think I understand what you</p> <p>3 mean by "briefing."</p> <p>4 Q Briefing to the court in claim -- claim</p> <p>5 construction; briefs and motions and papers that</p> <p>6 defendants filed with the court during the court's</p> <p>7 claim construction determination.</p> <p>8 A I don't know if I was provided -- I</p> <p>9 don't recall being provided that the -- I believe</p> <p>10 the components of that are excerpted -- there are</p> <p>11 certain components of -- if I understand what that</p> <p>12 document is -- that are in the claim construction.</p> <p>13 Q Okay. And you were provided with the</p> <p>14 court's claim constructions; correct?</p> <p>15 A Yes.</p> <p>16 Q But regarding the court's claim</p> <p>17 constructions, were you provided with other</p> <p>18 arguments in paper form documents regarding the</p> <p>19 various parties' arguments they had made to the</p> <p>20 court before the court issued its claim</p> <p>21 construction orders?</p> <p>22 A I don't recall being provided those</p>	<p style="text-align: right;">Page 328</p> <p>1 A Uh-huh.</p> <p>2 Q -- you see that?</p> <p>3 A Uh-huh.</p> <p>4 Q Are these discussions with colleagues</p> <p>5 the same discussions from paragraph 35 of your</p> <p>6 opening report we discussed earlier today?</p> <p>7 A Yes.</p> <p>8 Q And there are no additional</p> <p>9 colleagues -- discussions with colleagues you</p> <p>10 relied upon to form the opinions in your rebuttal</p> <p>11 report?</p> <p>12 A Correct.</p> <p>13 Q And you go on to say that neurosurgeons</p> <p>14 using the products can see an observable change in</p> <p>15 the visualization agent and neurosurgeons use that</p> <p>16 observable change to determine when they have</p> <p>17 applied the particular thickness of the product</p> <p>18 that they previously had determined they wanted to</p> <p>19 apply.</p> <p>20 Do you see that?</p> <p>21 A Yes.</p> <p>22 Q And what specifically did you base that</p>
<p style="text-align: right;">Page 327</p> <p>1 documents.</p> <p>2 Q And you didn't rely upon those</p> <p>3 documents in forming your opinions in this report;</p> <p>4 correct?</p> <p>5 A Well, some of those documents are</p> <p>6 excerpted in the claim constructions, so strictly</p> <p>7 speaking, yes, I guess I did rely on them.</p> <p>8 Q But you -- you -- is it more accurate</p> <p>9 to say --</p> <p>10 A Portions --</p> <p>11 Q -- you relied --</p> <p>12 A -- of them.</p> <p>13 Q -- you relied on the court's claim</p> <p>14 construction that might have referenced those</p> <p>15 documents?</p> <p>16 A Yes.</p> <p>17 Q Staying with paragraph 18, the bottom</p> <p>18 of page 9, you identify your use of the DuraSeal</p> <p>19 product and your discussions with my colleagues</p> <p>20 who have used the Adherus product, and it spills</p> <p>21 over to page 10.</p> <p>22 Do --</p>	<p style="text-align: right;">Page 329</p> <p>1 opinion on?</p> <p>2 A My own experience fundamentally; my</p> <p>3 conversations and -- and interactions with my</p> <p>4 colleagues. I've -- I've participated in cases --</p> <p>5 multiple cases with my colleagues who have used</p> <p>6 the products. And the video demonstrates the use</p> <p>7 of one. I think we could -- the video being the</p> <p>8 video of the temporal lobectomy.</p> <p>9 So multiple things.</p> <p>10 Q But you've never used the Adherus</p> <p>11 product; correct?</p> <p>12 A Correct.</p> <p>13 Q And you've never accompanied one of</p> <p>14 your colleagues in a surgical procedure while</p> <p>15 they're using the Adherus product; correct?</p> <p>16 A That's correct.</p> <p>17 Q So then your limit -- your opinion on</p> <p>18 the Adherus product is limited to your discussions</p> <p>19 with your colleagues at VCU and your review of the</p> <p>20 two videos; correct?</p> <p>21 A Yes.</p> <p>22 Q The various terms that we discussed</p>

<p style="text-align: right;">Page 330</p> <p>1 previously -- "visualization agent," "observable 2 change," "predetermined thickness" -- your 3 understanding of those terms, have they -- do they 4 differ at all between your opening report and your 5 rebuttal report? 6 A No, not that I can identify. 7 Q Looking at paragraph 19 -- 8 A Uh-huh. 9 Q -- which begins a new section of your 10 rebuttal report, it's titled -- the section is 11 titled Examples 4 and 5 of U.S. 6,312,725 to 12 Wallace do not teach a biocompatible hydrogel. 13 Do you see that? 14 A Yes. 15 Q And is it fair to say -- to refer to 16 this as the Wallace patent? 17 A Yes. Thank you. 18 Q And when was the first time you became 19 aware of the Wallace patent? 20 A Sometime in the period -- I mean, 21 that's -- certainly you should isolate the time 22 period between August 24th -- or I should say</p>	<p style="text-align: right;">Page 332</p> <p>1 particular when evaluating hydrogel sealants that 2 could be used in neurosurgical applications. 3 Do you see that? 4 A Yes. 5 Q And you're making this statement from 6 your experience as a -- as a neurosurgeon; 7 correct? 8 A Yes. 9 Q Is there any other expertise that 10 you're relying upon to make this statement? 11 A Not -- unless you're separating out 12 physicians in general from neurosurgeons, no, I 13 don't think there is. 14 Q No, we're not try- -- so -- 15 A Okay. 16 Q Is it your -- your -- your experience 17 as a neurosurgeon and -- and -- imported to 18 physicians in general as you can as a 19 neurosurgeon, that's the basis of the opinion your 20 [verbatim] express; correct? 21 A Yes. 22 Q And when you say a biocompatible</p>
<p style="text-align: right;">Page 331</p> <p>1 September 8th and October -- October 2nd, 2017. 2 Q So before the time that the opening 3 reports were filed in this litigation, you're 4 not -- you weren't aware of the Wallace patent? 5 A I don't recall that. 6 Q And how did the Wallace patent come to 7 your attention? 8 A In conversations with counsel. 9 Q Was it in relation with Dr. Lowman's 10 opening report in this investigation? 11 A It may have been, yes. 12 Q Were there -- would there be other 13 reasons that you're awareness of the Wallace 14 patent might have been -- come to your attention? 15 A Not that we -- none other than we've 16 just discussed. 17 Q Moving to paragraph 20, it states at 18 the beginning, The overarching requirement in the 19 claims in the '5,705 patent of having a 20 biocompatible hydrogel (as well as a biocompatible 21 first and second precursors) is well understood by 22 physicians in general and neurosurgeons in</p>	<p style="text-align: right;">Page 333</p> <p>1 hydrogel as well as biocompatible first and second 2 precursors, in your experience as a neurosurgeon, 3 if you have biocompatible first and second 4 precursors, would you also have a biocompatible 5 hydrogel? 6 A One would expect that, but I don't 7 think that's a certainty. 8 Q In your experience as a neurosurgeon, 9 why do you not think that's a certainty? 10 A Well, there aren't many certainties in 11 life, first of all. And there may be a 12 combination of things that are biocompatible which 13 when combined become nonbiocompatible. I 14 certainly think that's a -- a possibility. 15 Q Referring to biocompatible, if we look 16 at paragraph 21 and -- 17 A Twenty-one. 18 Q -- it states, The Wallace patent 19 defines biocompatible, and it gives a definition. 20 A Yes, sir, I'm there. 21 Q Do you agree with that definition of 22 biocompatible?</p>

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1 A The one that begins, quote, The ability
2 of the compositions?
3 **Q Correct.**
4 A Yes, I do.
5 **Q And in the -- the opinions expressed in**
6 **your report, you use the same definition of**
7 **biocompatibility as applied to all your opinions**
8 **in the report; is that correct?**
9 MR. ALTHERR: Object to form.
10 THE WITNESS: I use it -- yes, I
11 believe that's true.
12 BY MR. HUGHES:
13 **Q So you used -- the same opinion applies**
14 **uniformly throughout your report; is that correct?**
15 A I think you asked --
16 MR. ALTHERR: Object --
17 THE WITNESS: -- I --
18 MR. ALTHERR: -- to the --
19 THE WITNESS: -- if I --
20 MR. HUGHES: -- form.
21 THE WITNESS: -- used the same
22 definition.

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1 BY MR. HUGHES:
2 **Q Yes, the same definition part.**
3 A Yes, I used the -- I used that
4 definition that we just read --
5 **Q Okay. So --**
6 A -- from paragraph 21 in quotations.
7 **Q Okay. So you -- you -- the -- the**
8 **definition applied from the Wallace patent is a**
9 **definition that you have applied for the**
10 **definition of biocompatibility; is that correct?**
11 MR. ALTHERR: Object to the form.
12 THE WITNESS: I would accept it as a
13 definition of biocompatibility, yes.
14 BY MR. HUGHES:
15 **Q And is that the definition that you**
16 **used when forming your opinions expressed in this**
17 **report?**
18 MR. ALTHERR: Object to the form.
19 THE WITNESS: Your question, if -- if I
20 can clarify, is this definition in quote -- quoted
21 in paragraph 21, which includes table 3, is this
22 the definition that I -- I used to define

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1 biocompatibility in this rebuttal report?
2 BY MR. HUGHES:
3 **Q That's my question.**
4 A Yes.
5 **Q And you used that definition uniformly**
6 **throughout your report; is --**
7 MR. ALTHERR: Object --
8 BY MR. HUGHES:
9 **Q -- that accurate?**
10 MR. ALTHERR: -- to the form.
11 THE WITNESS: I don't know if that's
12 accurate. I --
13 BY MR. HUGHES:
14 **Q Well, did you change the definition you**
15 **applied?**
16 A Not intentionally. I did not.
17 **Q Okay. Looking at paragraph 20, the --**
18 **at the top of page 11, there's a bolded section at**
19 **the bottom of a quote paragraph that says, The**
20 **biocompatibility of the implant was assessed by**
21 **standard histological techniques.**
22 **Do you see that?**

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1 A Yes.
2 **Q Is it your understanding that**
3 **pathologists perform histological techniques?**
4 A Yes.
5 **Q Do neurosurgeons typically perform**
6 **histological techniques?**
7 A Histological techniques refers to the
8 microscopic evaluation of tissues usually under a
9 microscope, sometimes under another type of
10 magnification device, to determine anatomy. And
11 on a routine basis, for example, when malignancies
12 are examined histologically, the examination
13 certainly includes a neurosurgeon.
14 For example, any time I do a biopsy or
15 tumor resection, I'll routinely review the
16 histology. Another example will be during
17 management conferences of malignancies or
18 infections, we review the histology. Another
19 example would be that part of the -- the written
20 board examination for neurological surgeons
21 concerns histology.
22 So, yes, it is a significant

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1 component -- it is a component of neurosurgical
 2 practice.
 3 **Q But the component of neurosurgical**
 4 **practice is -- is it fair to say that it's**
 5 **analyzing the results of the histological process?**
 6 MR. ALTHERR: Object to the form.
 7 THE WITNESS: I think all histological
 8 practice is analyzing histological processing.
 9 BY MR. HUGHES:
 10 **Q But the actual processing of the**
 11 **sample -- staining it, preparing it -- do**
 12 **neurosurgeons typically perform that function?**
 13 A They do not. That's typically
 14 performed by a cytotechnician or a
 15 histotechnician.
 16 **Q Are those versions of pathologists?**
 17 A No.
 18 **Q Are you an expert in the cytotechnician**
 19 **or -- is it an endotechnician you mentioned?**
 20 A Either of those -- they're technicians
 21 that prepare and --
 22 **Q Okay.**

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1 A -- perform the staining, and, no, I'm
 2 not.
 3 **Q And you're not a pathologist; correct?**
 4 A That's correct.
 5 **Q Is it fair to say that your expertise**
 6 **as a neurosurgeon is more on analyzing the results**
 7 **of what the technicians would do versus processing**
 8 **the sample itself?**
 9 MR. ALTHERR: Object to the form.
 10 THE WITNESS: I think it's more common
 11 to analyze the results of a pathologist, not the
 12 technicians.
 13 BY MR. HUGHES:
 14 **Q So the technicians perform a function,**
 15 **and then the pathologists --**
 16 A Performs an analysis.
 17 **Q Analysis.**
 18 **And you analyze the pathologist's**
 19 **analysis?**
 20 A Or analyze it with the pathologist.
 21 As I said, we -- the examination of a
 22 tumor specimen, just to use an example, that's

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1 done in a multidisciplinary fashion on a routine
 2 basis as part of management.
 3 **Q Are you familiar with the project**
 4 **Coseal, C-O-S-E-A-L?**
 5 A I'm not.
 6 **Q If I represented to you that it's a**
 7 **surgical product from Baxter, would that be**
 8 **surprising?**
 9 A A surgical product from Baxter?
 10 **Q Yeah.**
 11 A No, I would not be surprised.
 12 **Q I believe it's used for vascular**
 13 **reconstruction.**
 14 A You spelled it C-O-S-E-A-L; is --
 15 **Q I --**
 16 A -- that --
 17 **Q -- believe --**
 18 A -- correct?
 19 **Q -- that's the spelling.**
 20 A Okay.
 21 **Q Coseal.**
 22 **In paragraph 23 -- 22 of your report,**

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1 **and it moves on to 23, you look at table 4 of the**
 2 **Wallace patent, and you express an opinion that a**
 3 **neurosurgeon would not want to use Test C due to**
 4 **bioincompatibility issues.**
 5 **Do you see that?**
 6 A Yes.
 7 **Q And that's because paragraph 23 states,**
 8 **"In my opinion, the result showing severe foreign**
 9 **body response and severe inflammation would**
 10 **indicate" -- and I -- a neurosurgeon would not**
 11 **want to use that due to bioincompatibility; is**
 12 **that accurate?**
 13 A Yes.
 14 **Q Then moving on to paragraph 26, you**
 15 **address Test D of the Wallace patent.**
 16 **Do you see that?**
 17 A Yes.
 18 **Q And is Test D and Test C -- those are**
 19 **shown in table 4 here on page 12 of your report.**
 20 **Do you see that?**
 21 A Yes.
 22 **Q And they have indications on table 4**

<p style="text-align: right;">Page 342</p> <p>1 indicating some level of bioincompatibility.</p> <p>2 Do you see that?</p> <p>3 A Yes.</p> <p>4 Q So moving back to paragraph 26 and Test</p> <p>5 D, you provide the opinion that a neurosurgeon --</p> <p>6 there's a quote here five lines from the bottom:</p> <p>7 A neurosurgeon, presented with such testing, would</p> <p>8 characterize the hydrogels as not being</p> <p>9 biocompatible and not want to use them in a</p> <p>10 medical procedure.</p> <p>11 Do you see that?</p> <p>12 A Yes.</p> <p>13 Q So is it your opinion that the results</p> <p>14 of Test D, a surgical -- a neurosurgeon would not</p> <p>15 want to use in a medical procedure?</p> <p>16 A I think -- correct.</p> <p>17 Q And if Test D actually was an</p> <p>18 FDA-approved product for use in medical</p> <p>19 procedures, would that affect your opinion in</p> <p>20 paragraph 26?</p> <p>21 A You ask a hypothetical question; the</p> <p>22 answer is it could.</p>	<p style="text-align: right;">Page 344</p> <p>1 use a hypothetical example -- that a product has</p> <p>2 FDA approval for vascular reconstruction.</p> <p>3 With that information, would you still</p> <p>4 believe that Test D is not suitable for a medical</p> <p>5 procedure?</p> <p>6 A Well, no.</p> <p>7 MR. ALTHERR: Object to the form.</p> <p>8 THE WITNESS: No, because in the</p> <p>9 hypothetical example you stated, you've explained</p> <p>10 that the hypothetical device was approved by the</p> <p>11 FDA for a medical procedure which would imply that</p> <p>12 the FDA and the advisors had -- were satisfied</p> <p>13 that for the on-label application of that device</p> <p>14 it was acceptable to use.</p> <p>15 So although this is a hypothetical</p> <p>16 example and this is a different circumstance --</p> <p>17 the example you gave is a vascular procedure -- I</p> <p>18 wouldn't judge just based on what you told me that</p> <p>19 it was unacceptable to use in a medical procedure</p> <p>20 if it was FDA approved for that purpose.</p> <p>21 BY MR. HUGHES:</p> <p>22 Q So it would be your opinion if it was</p>
<p style="text-align: right;">Page 343</p> <p>1 Q Yeah.</p> <p>2 So in the hypothetical example, if Test</p> <p>3 D was shown to be the same product of an</p> <p>4 FDA-approved product for use in medical condition,</p> <p>5 that would affect your opinion?</p> <p>6 MR. ALTHERR: Object to the form.</p> <p>7 THE WITNESS: It could, yes.</p> <p>8 BY MR. HUGHES:</p> <p>9 Q And if the FDA -- let's hypothetically</p> <p>10 say it's for vascular reconstruction procedures.</p> <p>11 And if the FDA had approved that, would you still</p> <p>12 think it's appropriate -- not appropriate for use</p> <p>13 in a medical procedure?</p> <p>14 A You're asking me in the hypothetical</p> <p>15 example that a device having a profile -- can you</p> <p>16 repeat it, please --</p> <p>17 Q Uh-huh.</p> <p>18 A -- rather than me trying to rephrase</p> <p>19 it?</p> <p>20 Q Yeah. Of course.</p> <p>21 Hypothetical example -- because you're</p> <p>22 not familiar with the Coseal products, so we'll</p>	<p style="text-align: right;">Page 345</p> <p>1 FDA approved for that purpose it would be</p> <p>2 appropriate to use it for that purpose?</p> <p>3 MR. ALTHERR: Object to form.</p> <p>4 THE WITNESS: I can't -- yes. I can't</p> <p>5 think of an example where an FDA-approved device</p> <p>6 for a particular indication I'm of the opinion is</p> <p>7 inappropriate or a bad idea or -- or -- or not</p> <p>8 indicated or something that neurosurgeons would</p> <p>9 not do.</p> <p>10 BY MR. HUGHES:</p> <p>11 Q And is it your opinion applying the</p> <p>12 same definition of bioincompatibility if it was</p> <p>13 FDA approved for -- if there was a sealant that</p> <p>14 was FDA approved for use in the human body that it</p> <p>15 would not be appropriate for a medical procedure?</p> <p>16 MR. ALTHERR: Object to the form.</p> <p>17 THE WITNESS: So now you're making an</p> <p>18 extrapolation from a vascular device,</p> <p>19 hypothetically, to a dural sealant.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q I gave a different hypothetical.</p> <p>22 A That was the only change I noticed;</p>

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1 that it was -- is a dural sealant now.

2 **Q I believe I said sealant, but --**

3 A Okay. Sealant.

4 So you extrapolated if a dural sealant

5 had that profile for biocompatibility as example

6 D.

7 **Q Uh-huh.**

8 A That's what you're asking?

9 **Q That's one hypothetical. Let's go with**

10 **that.**

11 A Yeah, and that's -- that's a completely

12 different scenario, and I would again have

13 concerns.

14 Your hypothetical example of -- of --

15 of a vascular device -- I don't know anything

16 about this device because it's hypothetical. But

17 there are -- there are devices -- there are things

18 that result in inflammation intentionally that we

19 accept and may even want to happen. That is far

20 from the situation in dural sealants or sealants.

21 So the standard of biocompatible that

22 we might accept -- I'm going to rephrase a little

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1 bit or phrase it a different way or explain a

2 different way.

3 The standard for biocompatibility or

4 tolerance for histological evidence of

5 inflammation is very different in some clinical

6 situations than others, and adjacent to the neural

7 elements on the dura is one that the -- the

8 tolerance is low for any amount.

9 **Q And in a hypothetical, if it was FDA**

10 **approved as a sealant for another -- a sealant in**

11 **general, would that affect your opinion on its use**

12 **for a medical procedure?**

13 MR. ALTHERR: Object to the form.

14 THE WITNESS: I don't understand your

15 question.

16 BY MR. HUGHES:

17 **Q Well, your opinion here is a**

18 **neurosurgeon presented with such tasking would**

19 **characterize a hydrogel as not being biocompatible**

20 **and not wanting to use them in medical -- in a**

21 **medical procedure.**

22 A Correct.

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1 **Q So that's what I'm looking at with the**

2 **hypothetical.**

3 A What's the question?

4 **Q That if it was an FDA approval as a**

5 **sealant, would that affect your opinion regarding**

6 **its appropriateness for use in a medical**

7 **procedure?**

8 MR. ALTHERR: Object to the form.

9 THE WITNESS: Define "sealant." You

10 need to define sealant for me.

11 So there are sealants that may be FDA

12 approved for one anatomical location or one

13 application or one situation that would be wholly

14 unacceptable as dural sealants.

15 BY MR. HUGHES:

16 **Q And it's your opinion that Test D in**

17 **Wallace is unacceptable as a dural sealant?**

18 A Yes.

19 **Q And what is the basis of that opinion?**

20 A The -- the graded inflammation results

21 in table 4 regarding the degree of

22 biocompatibility they have.

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1 **Q And are there any other bases expressed**

2 **in your report for that opinion?**

3 A I mean, I'm not excluding table 3.

4 Only what's in the paragraphs 21 through 26, and

5 the biocompatibility issue continues in 27, 28.

6 **Q Referring to paragraph 27, this**

7 **addresses barium sulfate, I believe.**

8 A Yes.

9 **Q Have you ever used barium sulfate in a**

10 **hydrogel?**

11 A No.

12 **Q Have you ever used barium sulfate in a**

13 **GI tract in a procedure?**

14 A Yes.

15 **Q In what procedure have you used barium**

16 **sulfate in the GI tract?**

17 A Modified barium swallow examination.

18 **Q Okay. And in your opinions expressed**

19 **in paragraph 27 through 32, you address the**

20 **toxicity to human tissue.**

21 **Do you see that? It's about five or**

22 **six lines down in paragraph 27.**

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1 A Yes.

2 **Q In your opinion expressed in your**

3 **rebuttal report, do you address the concentration**

4 **of the product in relation to toxicity to human**

5 **tissue?**

6 A I don't believe so, no.

7 **Q Have you ever studied the toxicity of**

8 **barium sulfate?**

9 A I studied this topic in preparation for

10 this deposition.

11 **Q Apart from your experience in this**

12 **litigation, have you ever studied the toxicity of**

13 **barium sulfate?**

14 A Yes. The -- yes, I have.

15 **Q And how so?**

16 A There are situations where the use of

17 contrast agents is or isn't used during the

18 evaluation of trauma patients prior to CT scans,

19 prior to the evaluation of bowel obstructions; and

20 there are times when we -- when it's advisable not

21 to use it because of concern of spillage outside

22 the GI tract, and I certainly have studied that

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1 previously in my career.

2 **Q And as a neurosurgeon, do you often**

3 **deal with CT scans of the GI tract?**

4 A I would say more than 95 percent of the

5 trauma patients -- the answer is yes --

6 **Q Okay.**

7 A -- and I can expand on that.

8 More than 20 -- more than 95 percent,

9 if not all, of the trauma patients, for example,

10 that we deal with and treat receive CT scans of

11 their chest, abdomen and pelvis to include their

12 GI systems.

13 **Q And it's trauma patients because**

14 **something happened presumably that has multiple**

15 **indications in their body. One of -- would**

16 **require a neurosurgeon and others would require**

17 **something else within the body?**

18 A Correct.

19 **Q So that's an adjunct to your expertise**

20 **as a neurosurgeon; is that accurate?**

21 A I don't know if I would agree with that

22 wording, but --

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1 **Q As a neurosurgeon, you don't primarily**

2 **focus on the treatment of GI tract issues?**

3 A That's correct.

4 **Q And the application of barium sulfate**

5 **in the GI tract is not within the primary focus of**

6 **your role as a neurosurgeon?**

7 A No, that -- that's true. It is not

8 within my primary focus as a neurosurgeon. I

9 agree with that statement.

10 **Q So your studying of the toxicity of**

11 **barium sulfate is more of a general -- is more of**

12 **a -- your role of a general doctor than a**

13 **neurosurgeon?**

14 MR. ALTHERR: Object to the form.

15 THE WITNESS: And I -- I would -- no,

16 not necessarily.

17 I'll give you another example. It is

18 routine for patients with stroke, which is a

19 very -- I care for hundreds of them a year. And

20 it is routine that they receive barium studies to

21 evaluate their swallow or other studies to include

22 their GI function. And there are situations where

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1 they have documented evidence of GI dysfunction,

2 swallowing problems after their stroke.

3 They're under my care, and they -- it

4 is relevant to our practice in care of those

5 patients, so --

6 BY MR. HUGHES:

7 **Q Have you ever studied a toxicity of**

8 **barium sulfate in a human tissue other than the GI**

9 **tract?**

10 A I recall reading about the toxicity of

11 barium in the lungs -- in the pulmonary --

12 **Q When was --**

13 A -- system.

14 **Q -- that?**

15 A I couldn't give you an exact time.

16 Certainly in the last three years.

17 **Q And what were the details of the**

18 **toxicity of barium in the lungs?**

19 A It's bad.

20 **Q Do you know the concentration that was**

21 **addressed then?**

22 A The things I was reading addressed the

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1 standard concentrations for oral contrasts, and
 2 off the top of my head without it in front of me,
 3 no, I can't cite you on. It would be a standard
 4 available oral contrast concentration.
 5 **Q Okay. But you didn't study the effect**
 6 **of various levels of concentrations on the**
 7 **toxicity of human tissue outside of the GI tract?**
 8 A I agree with that statement.
 9 **Q Looking at paragraph 29, in the**
 10 **statements in paragraph 29 you say, I**
 11 **understand -- the second sentence in, I understand**
 12 **that the hydrogels made using a 1.5 weight percent**
 13 **of barium sulfate added to the mean component of**
 14 **the Adherus DuraSeal kit and a 4-arm PEG with a**
 15 **molecular weight of 5 grams per mol was**
 16 **substituted for the colored Adherus PEG.**
 17 **I believe PEG is pronounced Peg; is**
 18 **that accurate?**
 19 A Yes.
 20 **Q And do you see that sentence there?**
 21 A It's kilogram.
 22 But, yes, I followed -- I read the

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1 sentence with you.
 2 **Q What is this understanding based on?**
 3 A The details of the mixture used in the
 4 video that were provided to me.
 5 **Q And you were provided with the details**
 6 **of what was in the mixture of the video that was**
 7 **provided to you?**
 8 A I believe that's correct, yes.
 9 **Q And did you cite the details of those**
 10 **mixture in this report?**
 11 A I think that's what we just read.
 12 That's what I was referring to.
 13 **Q Yeah.**
 14 **So this wasn't another document that**
 15 **you cited as support for this report; it's just**
 16 **something you incorporated in paragraph 29?**
 17 A (Witness reviews document.)
 18 I can't recall the -- another place
 19 that it's -- that I cited it.
 20 **Q But the underlying foundation for that**
 21 **belief, it's not in another document cited in the**
 22 **report; it was given to you in another method and**

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1 **put into the body of the report?**
 2 A It may be in a document that is cited
 3 here. I just can't off the top of my head
 4 identify that document.
 5 **Q And we discussed earlier you didn't**
 6 **perform any -- any of these experiments yourself,**
 7 **did you?**
 8 A That's correct. I did not.
 9 **Q And do you know what a 4-arm PEG is?**
 10 A A 4-arm PEG is not something that I
 11 have expert knowledge of but is a great example of
 12 the kind of thing to -- that I discussed with
 13 Dr. Mays.
 14 **Q But earlier I thought you said you**
 15 **didn't rely upon any of your opinions in this**
 16 **report with your discussions with Dr. Mays?**
 17 A I did. That's correct. I did say
 18 that.
 19 **Q But now you're saying what a 4-arm PEG**
 20 **is. So if you wanted to find out what a 4-arm PEG**
 21 **was, you would talk to Dr. Mays about it?**
 22 A Exactly. And I think discussion of

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1 structure of PEG -- different PEG moieties was
 2 definitely part of our discussion that I had with
 3 Dr. Mays originally.
 4 **Q Back in your one-hour --**
 5 A Correct.
 6 **Q -- discussion --**
 7 A Yes.
 8 **Q -- with him?**
 9 A Yes.
 10 I'm sorry to talk over you.
 11 Yes. Correct.
 12 **Q But you didn't feel you needed to**
 13 **understand what a 4-arm PEG was to opine on the**
 14 **issues you opined on in this report; is that**
 15 **accurate?**
 16 A That --
 17 MR. ALTHERR: Object to form.
 18 THE WITNESS: That's correct.
 19 BY MR. HUGHES:
 20 **Q Looking at page 30.**
 21 A Page 30.
 22 **Q Pardon me. Paragraph 30.**

<p style="text-align: right;">Page 358</p> <p>1 A Okay. Paragraph 30.</p> <p>2 Q Midway down you state -- seven</p> <p>3 sentences down, My opinion -- In my opinion, the</p> <p>4 barium sulfate did not provide a means for</p> <p>5 visualization of the coating or suitable</p> <p>6 visualization agent as a neurosurgeon would want</p> <p>7 to see that the barium sulfate was evenly</p> <p>8 distributed at the point of application of the</p> <p>9 hydrogel and not unpredictably applied in clumps.</p> <p>10 Do you see that?</p> <p>11 A Yes.</p> <p>12 Q When you say unpredictably applied in</p> <p>13 clumps, what do you mean by that?</p> <p>14 A In the video I think it -- it does a</p> <p>15 better job of explaining -- of demonstrating what</p> <p>16 is meant by that.</p> <p>17 But instead of flowing out in a</p> <p>18 symmetrically -- in a constant rate smoothly, et</p> <p>19 cetera, it comes out in -- at a varying rate with</p> <p>20 certain portions where it's thin and coming out</p> <p>21 quickly and other parts where big, thick chunks</p> <p>22 are coming out.</p>	<p style="text-align: right;">Page 360</p> <p>1 A Yes, I believe they came out in a much</p> <p>2 different fashion than the barium sulfate</p> <p>3 material.</p> <p>4 Q And, so, they came out in a smooth</p> <p>5 fashion instead of a -- how would you describe the</p> <p>6 barium sulfate came out?</p> <p>7 A Unpredictably.</p> <p>8 Q Is that accurate that the Adher- -- in</p> <p>9 your view the Adherus product in those two videos,</p> <p>10 that came out in a smooth fashion?</p> <p>11 A Came out predictably in a different</p> <p>12 manner. Yes, I agree with that.</p> <p>13 Q Now contrasting that to your use of the</p> <p>14 DuraSeal product, does the DuraSeal product come</p> <p>15 out in clumps and fits or does that come out in a</p> <p>16 smooth and predictable manner?</p> <p>17 MR. ALTHERR: Object to the form.</p> <p>18 THE WITNESS: No, in general the</p> <p>19 DuraSeal also comes out in a predictable manner.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q When applying a DuraSeal product, have</p> <p>22 you ever applied more than you may have wanted due</p>
<p style="text-align: right;">Page 359</p> <p>1 Q And when you say "coming out," you mean</p> <p>2 coming out of the applicator?</p> <p>3 A That's right. Being applied -- during</p> <p>4 the application.</p> <p>5 Q So it's some portions of big -- lots of</p> <p>6 material coming out and then little material and</p> <p>7 lots of material coming out of the applicator?</p> <p>8 A That's right. It's not up -- it</p> <p>9 doesn't come out in a smooth, constant manner.</p> <p>10 Again, I may be doing an imperfect</p> <p>11 effect job of explaining it, but the video, I</p> <p>12 think, would demonstrate it well.</p> <p>13 Q And in your review of the video of the</p> <p>14 Adherus product being applied, did the Adherus</p> <p>15 product come out in a smooth and constant manner?</p> <p>16 A Which video do you mean?</p> <p>17 Q Both videos that you referenced earlier</p> <p>18 about the Adherus product.</p> <p>19 There's two videos; correct?</p> <p>20 A The temporal lobectomy and then the --</p> <p>21 and then the demonstration teaching video?</p> <p>22 Q Correct.</p>	<p style="text-align: right;">Page 361</p> <p>1 to the applicator?</p> <p>2 A I can't think of a time.</p> <p>3 Q Have you ever had a DuraSeal product</p> <p>4 clog on you while you're using it?</p> <p>5 A Yes. I think you've asked that</p> <p>6 previously, and I've answered yes.</p> <p>7 Q And have you ever had a DuraSeal</p> <p>8 product where more -- more material than you would</p> <p>9 expect comes out at various times in the</p> <p>10 application?</p> <p>11 MR. ALTHERR: Object to the form.</p> <p>12 THE WITNESS: Not that I can recall.</p> <p>13 BY MR. HUGHES:</p> <p>14 Q Not that you can recall.</p> <p>15 Are you aware of other surgeons having</p> <p>16 problems with the DuraSeal product due to its</p> <p>17 smoothness of application?</p> <p>18 A I'm not, no.</p> <p>19 Q No.</p> <p>20 So you're not aware of any criticisms</p> <p>21 of the DuraSeal product based on the smoothness of</p> <p>22 its application?</p>

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1 MR. ALTHERR: Object to the form.
 2 THE WITNESS: Correct.
 3 BY MR. HUGHES:
 4 **Q How many times have you used the**
 5 **DuraSeal product?**
 6 A Certainly hundreds.
 7 **Q And would you say that in your hundreds**
 8 **of use the DuraSeal product has evenly, smoothly**
 9 **come out in your applications?**
 10 A Yes.
 11 **Q In all of your applications?**
 12 A Yes.
 13 **Q How do you define the even and**
 14 **smoothness of the DuraSeal product in its**
 15 **application?**
 16 A That with a -- that there's a
 17 correlation, for example, between the speed or
 18 pressure that one applies if -- to the applicator
 19 and the rate at which it responds to that
 20 pressure. So that if you apply very light
 21 pressure, there isn't all of the sudden a sudden
 22 gush of material; or, conversely, if it takes --

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1 that it comes out in an unpredictable manner.
 2 **Q In your experience using the DuraSeal**
 3 **product, you've always had a correlation between**
 4 **the amount of pressure you applied to the**
 5 **applicator and the amount of material that comes**
 6 **out?**
 7 A Right. If -- if you're getting to a --
 8 something we discussed earlier, that the tip can
 9 clog is the only exception to that where I don't
 10 think that's the smoothness of the application.
 11 But that's the only criticism I'm aware of that
 12 relates to your questions, and I've certainly
 13 experienced that as I have no doubt most DuraSeal
 14 users have.
 15 **Q But if the tip clogs, that's going to**
 16 **stop the application of the product; correct?**
 17 A That's correct.
 18 **Q So then that's going to stop the**
 19 **smoothness of the application of the product at**
 20 **the time the tip clogs; correct?**
 21 A No, I think -- I think those are two
 22 different things.

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1 **Q How are those two different things?**
 2 A Smoothness I'm using to describe when
 3 the materials is being applied, does it come out
 4 in a uniform rate, the same amount over a period
 5 of time.
 6 If a tip clogs, there's no material
 7 coming out.
 8 **Q But if you have a --**
 9 A There's no movement whatsoever to be
 10 smooth or not smooth.
 11 **Q But if you have material coming out and**
 12 **the tip clogs, that's an abrupt no material coming**
 13 **out while you're still applying pressure to the**
 14 **device; correct?**
 15 A For a short period of time, that's
 16 correct. It's a lack of material being delivered.
 17 **Q Isn't an abrupt stoppage of material**
 18 **being delivered amongst the definition of not**
 19 **being a smooth delivery?**
 20 MR. ALTHERR: Object to the form.
 21 THE WITNESS: Yeah, I guess it depends
 22 on your definition. What we're arguing about

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1 is -- or what we're discussing is the description
 2 of the word "smoothness" as applied to the
 3 application of DuraSeal.
 4 BY MR. HUGHES:
 5 **Q So in your opinion, application of**
 6 **DuraSeal is constantly smooth until you get no**
 7 **application whatsoever?**
 8 A If that happens.
 9 **Q And you've never experienced the**
 10 **applicator applying more material than you would**
 11 **expect based on the pressure of the applicator**
 12 **while you're applying DuraSeal?**
 13 A That's correct, not that I can recall.
 14 You're asking -- "more" is the word you used.
 15 **Q I said "more," yes.**
 16 A Okay.
 17 **Q So the converse of that, have you ever**
 18 **experienced less DuraSeal product coming out of**
 19 **the applicator based on the pressure you're**
 20 **applying than you'd normally expect?**
 21 A In those situations where the tip
 22 clogs, that's certainly less than one expects when

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1 you press it. So, yes, I would agree with that
 2 statement.
 3 **Q So in your opinion, the results of the**
 4 **barium sulfate video that you observed and**
 5 **discussed in paragraph 30, is it fair to say that**
 6 **the application of that barium sulfate material**
 7 **was nothing like the application of the DuraSeal**
 8 **product?**
 9 MR. ALTHERR: Object to form.
 10 THE WITNESS: Yes. Correct.
 11 BY MR. HUGHES:
 12 **Q And is that due to the applicator or is**
 13 **that due to the hydro -- hydrogel product itself?**
 14 A Is what due?
 15 **Q The lack of smoothness of the**
 16 **application.**
 17 A In the video?
 18 **Q Yes.**
 19 MR. ALTHERR: Object to the form.
 20 THE WITNESS: I have no idea what it's
 21 from.
 22 BY MR. HUGHES:

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1 **Q So your opinion is there is a lack of**
 2 **smoothness of the hydrogel, but you don't know**
 3 **whether it's due to the hydrogel itself or the**
 4 **applicator that's being used to apply it?**
 5 MR. ALTHERR: Object to form.
 6 THE WITNESS: That's correct. It would
 7 be speculative.
 8 BY MR. HUGHES:
 9 **Q That's referring to the video addressed**
 10 **in paragraph 30 of your report?**
 11 A Correct.
 12 **Q As a long time DuraSeal user, what are**
 13 **your understanding of the largest drawbacks of the**
 14 **DuraSeal product?**
 15 MR. ALTHERR: Object to the form.
 16 THE WITNESS: The tip clogging, and
 17 possibly cost if you can avoid using any dural
 18 sealant be it fiber and glue or -- or any product.
 19 It imparts additional cost to a procedure.
 20 BY MR. HUGHES:
 21 **Q Based on your discussions with other**
 22 **surgeons who use the DuraSeal product, other than**

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1 **cost of dural sealant at all and the tip clogging,**
 2 **what issues have they expressed to you as a less**
 3 **desirable trait of the DuraSeal product?**
 4 MR. ALTHERR: Object to the form.
 5 THE WITNESS: I can't think of any.
 6 BY MR. HUGHES:
 7 **Q Has anyone ever expressed to you a**
 8 **dissatisfaction with the application process other**
 9 **than tip clogging?**
 10 A Not that I can recall.
 11 MR. HUGHES: Let's do one more.
 12 (Deposition Exhibit 413 was marked for
 13 identification and attached to the transcript.)
 14 THE WITNESS: Thank you.
 15 BY MR. HUGHES:
 16 **Q Dr. Rivet, you've just been handed**
 17 **what's been marked as Exhibit 412 [sic]. It has a**
 18 **previous marker on it from Plaintiff's**
 19 **Exhibit 194, but today we'll be calling it**
 20 **Exhibit 412.**
 21 A I've got 413 on mine.
 22 **Q You're right. 413. Pardon me.**

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1 **You've been -- just been handed what's**
 2 **marked Exhibit 413. Have you seen this document**
 3 **before?**
 4 A I have not seen this document.
 5 **Q So if you could quickly flip through**
 6 **this document just a few pages.**
 7 A Sure.
 8 **Q You'll see at the bottom right-hand**
 9 **corner it says, Adherus AutoSpray Following**
 10 **Temporal Lobectomy.**
 11 A Yes.
 12 **Q Is it fair to say that this is a**
 13 **printout of the -- these are printouts from the**
 14 **video that you show some photos from in your**
 15 **report in paragraph 16?**
 16 A Yes, I think it is. I believe that to
 17 be true.
 18 **Q If you notice when you look at this**
 19 **video, there are screenshots at a certain time**
 20 **frame.**
 21 **Do you see that as you flip through the**
 22 **pages?**

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1 A Yes, I do see the time annotated on the
 2 bottom of each page.
 3 Q The -- the pictures you show in your
 4 report don't include the timestamp from each of
 5 these pictures.
 6 A They don't?
 7 Q The pictures you have in your report?
 8 A Oh --
 9 Q Look at --
 10 A -- I'll -- I'll --
 11 Q -- your --
 12 A -- have --
 13 Q -- rebuttal --
 14 A -- to go back.
 15 Q -- report --
 16 A Okay.
 17 Q -- in paragraph 16 --
 18 A Sure.
 19 Q -- and compare that with the example I
 20 have in my hand --
 21 A Okay.
 22 Q -- or Exhibit 413.

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1 A Paragraph 16. Okay. I have it, yes.
 2 You're --
 3 Q None of these -- so you testified that
 4 it's fair to say that this is a printout of the
 5 same video that you used photos of in paragraph 16
 6 of your rebuttal report.
 7 A And that I watched. I agree. I think
 8 that's true.
 9 Q And the handout I have here shows
 10 timestamps at the bottom; correct?
 11 A It does.
 12 Q But the -- the photos you use in your
 13 rebuttal report do not show timestamps at the
 14 bottom; correct?
 15 A That's true.
 16 Q Is there a reason you chose not to
 17 include the timestamps at the bottom for the
 18 photos you use in your -- your rebuttal report?
 19 A No reason in particular, no. It would
 20 make it more complete, I agree.
 21 Q Okay.
 22 A It is a nice feature of this handout.

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1 I mean . . .
 2 Q If you look at what's five pages into
 3 the handout -- it's not marked by pages, but the
 4 timestamp of the photos, 25 of 53 seconds.
 5 A I have that on.
 6 Q And you -- you'll see in these
 7 screenshot there's a white text that's been placed
 8 in some of the screenshots.
 9 Do you see that?
 10 A Yes, I do.
 11 Q And this white text says, Device was
 12 transferred to second student for an opportunity
 13 to use Adherus AutoSpray.
 14 Do you see that?
 15 A Yes, I do.
 16 Q So is it your understanding that at
 17 this point in the video the device was transferred
 18 to a different surgeon for that surgeon to get a
 19 chance to use the Adherus AutoSpray device?
 20 MR. ALTHERR: Objection: form.
 21 THE WITNESS: That's my understanding.
 22 I have no reason to doubt that.

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1 BY MR. HUGHES:
 2 Q If you look at the next page, it says
 3 the same thing, The device was transferred to a
 4 second surgeon.
 5 Do you see that?
 6 A Yes.
 7 Q And, admittedly, it's unclear if
 8 there's a third surgeon involved here or if there
 9 are just two surgeons involved.
 10 But is it fair to say there are at
 11 least two surgeons involved in this application of
 12 this procedure?
 13 A I think that's fair.
 14 Q Is it common in training environments
 15 for two surgeons to be applying the material in a
 16 given patient to do a hand-off like this video is
 17 purporting to do?
 18 A Certainly not unheard of at all.
 19 That's -- part of the, you know, supervised
 20 training is to demonstrate any technique and then
 21 in a supervised manner have the started maneuver,
 22 task, surgical step, be it application of this --

<p style="text-align: right;">Page 374</p> <p>1 this material or anything else, completed by the</p> <p>2 trainee or -- or a second surgeon.</p> <p>3 I don't know if the second surgeon was</p> <p>4 necessarily a trainee. We don't know that.</p> <p>5 Q So, yeah. I said "trainee," but the</p> <p>6 same would be for, you know, an exhibit of the</p> <p>7 device, correct, or a demonstration of the device</p> <p>8 in actual practice; that it's common for more than</p> <p>9 one surgeon to use a device?</p> <p>10 MR. ALTHERR: Object to the form.</p> <p>11 THE WITNESS: Yeah, I'm not sure I</p> <p>12 understand that.</p> <p>13 BY MR. HUGHES:</p> <p>14 Q So in -- in -- I used training as an</p> <p>15 example a --</p> <p>16 A Okay.</p> <p>17 Q -- second ago, and you said, well,</p> <p>18 you're not sure if it's training or not, but it's</p> <p>19 common in a training environment for one more than</p> <p>20 one person to use a device.</p> <p>21 A Yes, a hand-off as you called it.</p> <p>22 Q A hand-off.</p>	<p style="text-align: right;">Page 376</p> <p>1 I guess let me clarify. This video</p> <p>2 describes the device is transferred to a second</p> <p>3 surgeon. It is certainly not as common if there</p> <p>4 were two surgeons that were not trainees to have</p> <p>5 one surgeon start a portion of the procedure and</p> <p>6 then have a hand-off of the -- mid-procedure occur</p> <p>7 to a second surgeon.</p> <p>8 That's -- I'm sure it could occur and</p> <p>9 there might be a reason for it, but it's much less</p> <p>10 common outside of a training environment.</p> <p>11 Q That -- we --</p> <p>12 A Maybe --</p> <p>13 Q (Indicating).</p> <p>14 A No, I was just going to say maybe if it</p> <p>15 were a new device, for example, that neither</p> <p>16 surgeon had used, but they weren't trainees. If</p> <p>17 they were having a device introduced to their</p> <p>18 practice, maybe one would start a procedure and</p> <p>19 then hand it off to another one. So it's</p> <p>20 possible. It wouldn't concern me or be --</p> <p>21 Q So in either of these two scenarios, a</p> <p>22 new device entrant or a trainee entrant where more</p>
<p style="text-align: right;">Page 375</p> <p>1 And would it be expected that in other</p> <p>2 situations, a demonstration or other educational</p> <p>3 or learning environments, for a hand-off to pass</p> <p>4 to a different surgeon during a procedure?</p> <p>5 MR. ALTHERR: Object to the form.</p> <p>6 THE WITNESS: If I understand your</p> <p>7 question, other than an actual surgery, you're now</p> <p>8 something the same question in a training -- in</p> <p>9 a --</p> <p>10 BY MR. HUGHES:</p> <p>11 Q I'm asking context of an actual</p> <p>12 surgery.</p> <p>13 A Okay. I'm not sure how it's different</p> <p>14 from the first question, then.</p> <p>15 Q Well, you seem to have a problem with</p> <p>16 the word "training," so that's why I'm just say if</p> <p>17 train -- you know, in the context of training of</p> <p>18 the -- the context other than training a resident</p> <p>19 or a different trainee, if it's common to have</p> <p>20 more than one surgeon use the same device in an</p> <p>21 application for some other purpose?</p> <p>22 A I now understand. Sorry.</p>	<p style="text-align: right;">Page 377</p> <p>1 than one surgeon's using a device and, let's say,</p> <p>2 in the context of a dural sealant, would you</p> <p>3 expect the same application of the material when</p> <p>4 two surgeons are applying it versus when a</p> <p>5 singular surgeon is applying it?</p> <p>6 A Can you define "the same application of</p> <p>7 the material"?</p> <p>8 Q Well, the same procedure that you're</p> <p>9 applying material, would it be different when two</p> <p>10 surgeons are performing the same procedure versus</p> <p>11 a singular surgeon performing the procedure?</p> <p>12 MR. ALTHERR: Objection to form.</p> <p>13 THE WITNESS: I'm not sure I understand</p> <p>14 what you're -- what you're getting at, I guess.</p> <p>15 The difference would be there are two</p> <p>16 people doing it. It would involve a transfer of</p> <p>17 the material. Other than the obvious difference</p> <p>18 between two people doing it and one person doing</p> <p>19 it.</p> <p>20 BY MR. HUGHES:</p> <p>21 Q Is it fair to say you might have</p> <p>22 more -- more material applied when two people are</p>

<p style="text-align: right;">Page 378</p> <p>1 applying it in a training or demonstration</p> <p>2 environment than when a single surgeon is applying</p> <p>3 the material?</p> <p>4 A I don't agree with that statement.</p> <p>5 Q So when more than one surgeon is using</p> <p>6 the Adherus device in this video, isn't it fair to</p> <p>7 say that they might not be applying the material</p> <p>8 in the same way than if there was a singular</p> <p>9 surgeon using the material?</p> <p>10 MR. ALTHERR: Object to the form.</p> <p>11 THE WITNESS: No. In fact, I disagree.</p> <p>12 In fact, in the training environment, I think it's</p> <p>13 important that if I pass off the completion of a</p> <p>14 step to one of the resident trainees, I would</p> <p>15 expect that the result, be it the deposition of a</p> <p>16 dural sealant or any other, should resemble</p> <p>17 identically or as close as possible what the</p> <p>18 original -- again just taking this as example,</p> <p>19 what the original application of a dural sealant</p> <p>20 would look like or have been if I did it myself or</p> <p>21 a single surgeon did it themselves.</p> <p>22 Phrased another way, simply because of</p>	<p style="text-align: right;">Page 380</p> <p>1 it's a joint effort in assessing that or making</p> <p>2 that visual determination.</p> <p>3 Q You don't think it's fair to say the</p> <p>4 second person might apply more for the experience</p> <p>5 of using the product to apply more?</p> <p>6 A No, I don't think that would be</p> <p>7 appropriate particularly in the setting of an</p> <p>8 actual -- not -- not -- not particularly, but</p> <p>9 especially in the setting of an actual surgery in</p> <p>10 contradistinction to applying it to a -- the other</p> <p>11 video applying it to a piece of material ex vivo,</p> <p>12 have -- not involving the patient.</p> <p>13 Q And this is a type of a -- cranial</p> <p>14 surgery that's being shown in this exhibit; is</p> <p>15 that correct?</p> <p>16 A Yes, I believe that's correct.</p> <p>17 Temporal lobectomy is a cranial surgery.</p> <p>18 Q And is it fair to say that there is</p> <p>19 less of a concern for the overapplication of a</p> <p>20 dural sealant in a cranial procedure than in a</p> <p>21 spinal procedure?</p> <p>22 MR. ALTHERR: Object to form.</p>
<p style="text-align: right;">Page 379</p> <p>1 the involvement of two people, the goal in a</p> <p>2 training environment would be to be -- have there</p> <p>3 be no difference, and that's our role as</p> <p>4 supervising faculty in the training of surgeons.</p> <p>5 BY MR. HUGHES:</p> <p>6 Q You testified earlier that a user of</p> <p>7 Adherus would know to stop when there's an even,</p> <p>8 uniform coating of the Adherus applied; is that</p> <p>9 accurate?</p> <p>10 A Yes.</p> <p>11 Q So in this video example in this</p> <p>12 Exhibit 413, how would the first surgeon versus a</p> <p>13 second surgeon know when to stop applying the</p> <p>14 Adherus material?</p> <p>15 A The same way. By the visual change</p> <p>16 that they're -- you know, the visual change</p> <p>17 they're observing, and one could argue that there</p> <p>18 may be greater sensitivity with two sets of eyes</p> <p>19 than one sets of eye to judge that.</p> <p>20 So they could verbally communication</p> <p>21 during the application that, hey, do you think</p> <p>22 it's complete, or what do you think. It's a --</p>	<p style="text-align: right;">Page 381</p> <p>1 THE WITNESS: I agree with that.</p> <p>2 MR. HUGHES: I think we've been going</p> <p>3 about an hour. It's probably a good time to stop.</p> <p>4 MR. ALTHERR: Okay. How much longer do</p> <p>5 you think you're going to go?</p> <p>6 MR. HUGHES: Not long.</p> <p>7 THE VIDEOGRAPHER: The time is</p> <p>8 4:29:42 p.m. We are now off the record.</p> <p>9 (Recess -- 4:29 p.m.)</p> <p>10 (After recess -- 4:39 p.m.)</p> <p>11 THE VIDEOGRAPHER: This begins disk</p> <p>12 number 5 of the video deposition of Dennis Rivet,</p> <p>13 M.D. The time is 4:39 p.m. We are now on the</p> <p>14 record.</p> <p>15 BY MR. HUGHES:</p> <p>16 Q Dr. Rivet, during the break just now,</p> <p>17 did you discuss the substance of your testimony</p> <p>18 with counsel?</p> <p>19 A No.</p> <p>20 Q Have you discussed the substance of</p> <p>21 your testimony at any time during the breaks today</p> <p>22 with counsel?</p>

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1 A No.

2 MR. HUGHES: That's the end of my

3 questioning for today.

4 MR. ALTHERR: If that's the end of the

5 questioning, then that's the end of the

6 deposition.

7 The witness will read and sign.

8 THE VIDEOGRAPHER: This concludes the

9 video deposition of Dennis Rivet, M.D., consisting

10 of five DVD disks. The time is 4:39:37 p.m.

11 We are now off the record.

12

13 (Signature having not been waived, the

14 Videotaped Deposition of DENNIS JAMES RIVET, II,

15 M.D., ended at 4:39 p.m.)

16

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1 CERTIFICATE OF SHORTHAND REPORTER - NOTARY PUBLIC

2 I, Dana C. Ryan, Registered Professional

3 Reporter, Certified Realtime Reporter, the officer

4 before whom the foregoing proceedings were taken

5 do hereby certify that the foregoing transcript is

6 a true and correct record to the best of my

7 ability of the proceedings; that said proceedings

8 were taken by me stenographically and thereafter

9 reduced to typewriting under my supervision; and

10 that I am neither counsel for, related to, nor

11 employed by any of the parties to this case and

12 have no interest, financial or otherwise, in its

13 outcome.

14 IN WITNESS WHEREOF, I have hereunto set

15 my hand and affixed my notarial seal this 1st day

16 of November 2017.

17 My Commission expires:

18 July 15, 2020

19

20 _____

21 NOTARY PUBLIC IN AND FOR THE

22 DISTRICT OF COLUMBIA

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1 E R R A T A S H E E T

2 IN RE: INTEGRA LIFESCIENCES CORPORATION, et al.

3 v. HYPERBRANCH MEDICAL TECHNOLOGY, INC.

4 RETURN BY: _____

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1 E R R A T A S H E E T

2 IN RE: INTEGRA LIFESCIENCES CORP., et al. v.

3 HYPERBRANCH MEDICAL TECH., INC.

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DENNIS J. RIVET, II, M.D. - 10/27/2017

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